VOL. CLXI, No. 1 JANUARY, 1921 No. 586

1820 "A CENTURY OF SERVICE" 1921

THE

AMERICAN JOURNAL OF THE MEDICAL SCIENCES

GEORGE MORRIS PIERSOL, M.D., EDITOR
JOHN H. MUSSER, JR., M.D., ASSOCIATE EDITOR

THE LIBRARY OF CONGRESS SERIAL RECORD
JUL 26 1944

NOTES ON THE DIAGNOSIS OF BRONCHOPNEUMONIA AND ITS COMPLICATIONS. By NELLIS B. FOSTER, M.D. . . . . .

EXPERIMENTAL STUDIES IN DIABETES: SERIES II. THE INTERNAL PANCREATIC FUNCTION IN RELATION TO BODY MASS AND METABOLISM. II. CHANGES IN ASSIMILATION BY ALTERATIONS OF BODY MASS. By FREDERICK M. ALLEN, M.D. 16

BENZYL BENZOATE IN PEDIATRIC PRACTICE. By JOHN RUHRÄH, M.D. . . . 32

STUDIES IN THE PHYSIOLOGY OF THE LIVER: I. TECHNIC AND GENERAL EFFECTS OF REMOVAL. By F. C. MANN, M.D. 37

ALIMENTARY HYPERSECRETION; GASTRIC HYPERSECRETION; GASTROCHRONORRHEA. By BURRILL B. CROHN, M.D., and JOSEPH REISS, M.D. 43

OBSERVATIONS UPON THE TREATMENT OF THE CHRONIC INTESTINAL INVALID. By JOHN BRYANT, M.D. 63

ON THE ETIOLOGY OF TYPHUS FEVER. By EDWIN W. SCHULTZ, M.D. 78

ACUTE EPIDEMIC ENCEPHALITIS. By CHARLES H. MINER, M.D., and STANLEY L. FREEMAN, M.D. 91

RECURRENT TYPE I PNEUMONIA: SERUM TREATMENT OF TWO ATTACKS ONE MONTH APART. By HENRY M. THOMAS, JR., M.D. 103

THE COLLOIDAL GOLD CURVE IN EPIDEMIC ENCEPHALITIS: A PRELIMINARY NOTE. By THOMAS K. DAVIS, M.D., and WALTER M. KRAUS, M.D. 109

CARCINOMA OF THE SUPRA-AMPULLARY PORTION OF THE DUODENUM. By N. B. HERMAN, M.D., and WILLIAM C. VON GLAHN, M.D. 111

ETIOLOGY OF ACNE ROSACEA THROUGH A VISCERO-NEUROLOGIC MECHANISM. By FRANK PORTER MILLER, M.D. 120

INDEX TO ADVERTISERS . . . . . ADV. PAGE 18

Contents continued on page x

OWNERS AND PUBLISHERS
Philadelphia LEA & FEBIGER New York

COPYRIGHT, 1921, BY LEA & FEBIGER. ALL RIGHTS RESERVED. ENTERED AT THE POST-OFFICE AT PHILADELPHIA AS SECOND-CLASS MATTER

PUBLISHED MONTHLY. SUBSCRIPTION, SIX DOLLARS A YEAR, POSTPAID

Gonococcus Glycerol-Vaccine

Stable and Effective

Advantages:

1 - Will not deteriorate. 2 - Free from autolytic products.
3 - In preliminary trials has not produced toxic reactions even in large doses.

The types of cases reported to us as favorably influenced by Gonococcus Glycerol-Vaccine are chronic gonorrheal infections, including gonorrheal rheumatism, epididymitis, prostatitis and posterior urethritis.

Further Information on Request

LEDERLE ANTITOXIN LABORATORIES
511 FIFTH AVENUE NEW YORK

PNEUMOCOCCUS ANTIGEN

(Partially Autolyzed Pneumococci)

FOR *the* TREATMENT *of* PNEUMONIA

Prepared according to the method of Dr. E. C. Rosenow
Mayo Foundation

Indicated in the treatment of the primary infections due to pneumococci of the various types with resulting clinical lobar pneumonia.

The extensive use of Pneumococcus Antigen by physicians has more than justified the belief of Dr. Rosenow and his co-workers that the Antigen is of decided assistance in combating pneumococcus infections.

THE PACKAGE

Pneumococcus Antigen is supplied only in 5 c. c. rubber-capped ampoule vials (20 billion partially autolyzed pneumococci in each cubic centimeter). Order as V-903.

ELI LILLY & COMPANY

INDIANAPOLIS, U.S.A.

Hindle American Electrocardiograph

During the past year many of the most important institutions in the country have equipped themselves with the Hindle American Electrocardiograph.

The hospitals now find it necessary to include this apparatus as a valuable aid to their diagnoses, and no examination of the heart can be considered complete without an electrocardiogram.

New institutions should consider the wiring of the wards in making their future plans. Write us for particulars.

A representative list of institutions using our apparatus:

Bureau of Standards, Washington, D. C.
Cornell University Medical School, N. Y.
Johns Hopkins Hospital, Baltimore, Dept. of Medicine.
Medical Dept., U. S. Army (five equipments).
Government of Philippines, Manila, P. I.
Rockefeller Foundation, Brazil.
Michael Reese Hospital, Chicago.
Western Reserve University, Cleveland.
New York Hospital, N. Y.
Rockefeller Institute, N. Y.
Jefferson Medical College, Phila.
Bellevue Medical College, N. Y. City, etc.

MANUFACTURED BY

Charles F. Hindle

MAIN OFFICE AND FACTORY

(Formerly of 100 E. 126th St. New York City)

OSSINING, N. Y.

AMERICAN STANDARD
HAEMACYTOMETERS
WITH LEVY COUNTING CHAMBER

The Levy Counting Chamber was announced in November, 1916, patented January 31, 1917 (U. S. Patent No. 1,214,331) and was awarded the Edward Longstreth Medal of Merit by the Franklin Institute, Philadelphia, December, 1917

No. 29983. American Standard Haemacytometer with Levy Counting Chamber with double Neubauer ruling

THE LEVY COUNTING CHAMBER was the first dependable Haemacytometer Counting Chamber made in the U. S. and continues to be superior in several important characteristics to any chamber yet made either in Europe or America.

It provides an increased visibility of ruling when the chamber is filled, unequalled by any ruling of European make, and a new method of construction of the parallel form of cell (first suggested by Bürker) which entirely avoids the cemented cell of the Thoma or Bürker construction with the attendant danger of separation from the slide.

The parallel or open form of chamber permits the filling of the ruled area on the cover-glass by capillary attraction **after the cover-glass is in position on the slide,** and provides a more uniform distribution of the corpuscles than is possible with the Thoma or circular form of counting chamber which is entirely closed by the cover-glass.

The dimensions of the ruling and the depth of the cell are guaranteed to be within the tolerances established by the Bureau of Standards and, when so ordered, Counting Chambers are furnished with Bureau of Standards certificate at an additional price.

29991. American Standard Haemacytometer, complete with Levy Counting Chamber with Neubauer ruling, with two pipettes, in leather case **$15.00**

29992. American Standard Haemacytometer, same as 29991, with Bureau of Standards certificate **22.00**

29983. American Standard Haemacytometer, same as No. 29991, but with Levy Counting Chamber with double Neubauer ruling **18.00**

29984. American Standard Haemacytometer, same as 29983, with Bureau of Standards certificate **26.00**

Copy of Supplement No. 53, "American Standard Haemacytometers" sent on request

---

ARTHUR H. THOMAS COMPANY

WHOLESALE, RETAIL AND EXPORT MERCHANTS

LABORATORY APPARATUS AND REAGENTS

WEST WASHINGTON SQUARE **PHILADELPHIA, U. S. A.**

RADIUM

TO Physicians and Hospitals we offer Radium element of highest purity salts in form of Bromide or Sulphate. Sales are based upon certified measurement by the United States Bureau of Standards, Washington, D. C.

American mining properties owned by this Corporation supply our Radium-bearing ore and we control every mining, refining and laboratory operation in the production of our radium. This gives us complete knowledge of the purity which we guarantee.

We manufacture Needles, Applicators, Screens and special equipment for the therapeutic use of Radium.

THE

Radio Chemical Corporation

58 PINE STREET, NEW YORK

Telephone, John 3141

Plant and Laboratories
ORANGE, N. J.

Mines
COLORADO, UTAH

Gastron

"arrives"

For a long time GASTRON was "the thing beyond," the product-to-be—an extract of the entire stomach glands, alcohol-free. The idea that this would be of great interest and importance to the physician was persistent.

Now GASTRON, the reality, actually representative of the gastric gland tissue juice in active principles, in complex properties—obtained by acid-aqueous-extraction—has "arrived," through actual clinical trial, as a reliable and efficient resource in dealing with disorders of gastric function.

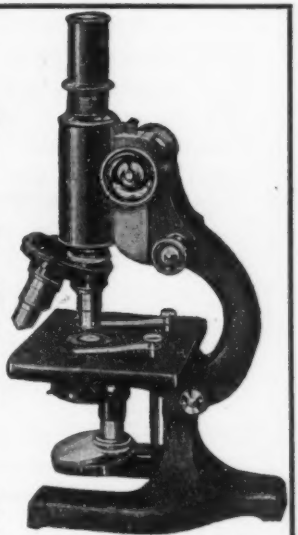
Fairchild Bros. & Foster
New York

SPENCER
Scientific Instruments

WHETHER
MICROSCOPES, MICROTOMES or DELINEASCOPES

Make an Instinctive Appeal to the Laboratory Worker

It isn't only their accuracy and utility. It's something in the finish, even more in the design; but in addition to all these, it is those little things—clever little devices, which accomplish the same end but in a better way—exactly the way the laboratory worker wants them. These are the distinctive features of the Spencer instruments, made distinctive because our designers—experienced laboratory workers, possess the laboratory view point.



Spencer Microscope No. 44

Spencer Microscope No. 44

has become a standard for university and college laboratory work. It is distinctive in that it has a side-fine adjustment with **34** threads of the screw always engaged instead of but **one** as in other makes. It has other advantages.

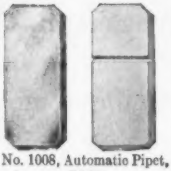
Send for Catalog

SPENCER LENS COMPANY
MANUFACTURERS
Microscopes, Microtomes, Delineascopes
BUFFALO, N. Y.

No. 1003
Candle and Electric Illumination. Attached to any Lamp Socket.
$40.00

DARE
HEMOGLOBINOMETERS

Examination of blood undiluted gives no chance for error, and makes for certainty in diagnosis.



No. 1008, Automatic Pipet, **$1.50**

Standard Equipment with Mayo Clinic, Army Medical School, U. S. Army, U. S. Public Health Service, etc.

WRITE TODAY FOR BOOKLET
For sale by leading supply houses

No. 1007—Candle illumination
$30.00

RIEKER INSTRUMENT COMPANY
1919 FAIRMOUNT AVENUE PHILADELPHIA, PA.

VIRGINIA HOT SPRINGS

Open All Year Round

WINTER days at this great American Spa are most pleasant and beneficial. Its "cure" provides every variety of scientific bath and hydrotherapeutic treatment. Natural waters of recognized potency work wonders, assisted by massage, Swedish gymnastics and the latest mechanical apparatus for corrective exercises.

AN enclosed viaduct leads from hotel to bath house. The luxurious Homestead,—2500 feet up in the Alleghanies—enjoys a Winter climate both mild and bracing. Sheltered, sunlit piazzas invite complete relaxation. Every facility for sport outdoors, every comfort and convenience within. Tempting Southern cuisine

Interesting and Informing Brochures on Request

THE HOMESTEAD

CHRISTIAN S. ANDERSEN
Resident Manager

Hot Springs, Va.

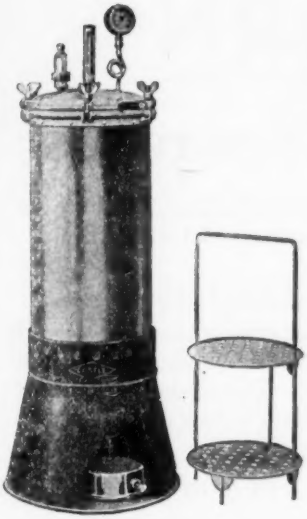
NEW YORK BOOKING OFFICE—THE RITZ-CARLTON

We Pay Cash FOR SINGLE MEDICAL BOOKS OR LIBRARIES. Send us list with author, title, and date of publication.

THE CHARLES T. POWNER CO., 26 E. Van Buren Street, Chicago, Ill.

BOOK-SELLERS and PUBLISHERS Stores in CHICAGO, CLEVELAND and LOS ANGELES

CASTLE AUTOCLAVES



New Pattern

THE sterilizing chamber is made with a seamless drawn copper shell—extra heavy to insure years of service. All riveting and soldering on the bottom and sides has been eliminated. Cover made of high-grade bronze

Offered now in the following sizes:

No. 461-A 8 x 12″
No. 471-A 11 x 24″
No. 481-A 14 x 26″

These autoclaves all have the cover hinged and are supplied complete with high-grade thermometer, safety valve and steam gauge. Gas, electric or oil heating.

Specify Castle Autoclaves when ordering through your supply house. Literature on request.

Wilmot Castle Company

1160 University Ave., ROCHESTER, N. Y.

Makers of the largest line of Sterilizers for laboratories, physicians, dentists and hospitals

HEALTH FOOD COMPANY

Established 1874 **By FRANK FULLER, M.D.**

Manufacturers of SIXTY-FIVE VARIETIES OF FOOD

These range from *absolutely starchless* Diabetic Casein Flour, Alpha Cracker, Almond Flour, Soy Bean and Soy Bean Flour to Proto Puffs, 3.26 per cent.—Pure Washed Gluten Flour, 3.77 per cent.—Proto Soy Wafers, 10.53 per cent., and a list of other foods up to the full starch tolerance diet.

Physicians are cordially invited to send for literature

HEALTH FOOD COMPANY

Retail Department **27 Lexington Avenue**
NEW YORK CITY

SANBORN

Metabolism Apparatus

Sanborn Instruments for Estimation of the Metabolic Rate have an Enviable Record for Satisfactory Performance in Actual Practice

Sanborn Benedict Metabolism Apparatus

Basal metabolism determinations of full clinical accuracy without gas analysis. In use and giving satisfactory service in hospitals and clinics and the offices of specialists, throughout the United States and several foreign countries.

"Handy Model" Metabolism Apparatus

A portable instrument for general practice. Complete in carrying case with oxygen tank, weighs less than 20 pounds. Invaluable in cases where the patient cannot be brought to the hospital or office. No gas analysis; no electrical connection.

Gasometer as Used at Mayo Clinic

For determination of the metabolic rate where exceptional accuracy is demanded. Requires the services of a skilled gas analyst. Recommended for the researchist and the institution where gas analysis is routine laboratory work.

In Using a Sanborn Apparatus, the Physician is not Experimenting with New and Untried Principles

---

Literature and Names of Users of Sanborn Metabolism Apparatus Gladly Sent Upon Request

---

SANBORN COMPANY

Makers of Scientific Instruments

1048 Commonwealth Avenue **BOSTON 47, MASS.**

HYCLORITE
CONCENTRATED
SODIUM
HYPOCHLORITE

Hyclorite Has Solvent Action

DRS. Austin and Taylor of Rockefeller Institute, New York, writing in the Journal of Experimental Medicine on "The Solvent Action of Antiseptics on Necrotic Tissue," state that "the solvent action of Dakin's Solution is due primarily to its hypochlorite content" and that "Dichloramine T and Chloramine T do not exhibit solvent action."

The same authorities have shown conclusively that a Dakin Solution made by dissolving chloramine tablets or powder is not alkaline and has no solvent action on necrosed tissue.

Hyclorite being of standardized hypochlorite strength and special alkalinity, ensures rapid solvent action. A Dakin's Solution can be made in one minute by merely adding the required amount of water to Hyclorite.

No waiting, filtering, titrating, or adding other chemicals, and the resulting solution is decidedly less irritating. Hyclorite has seven or eight times the strength of Dakin's Solution made in the usual way.

Hyclorite's concentration and preparation by special electro-chemic process assure its remarkable keeping qualities.

Hyclorite is Isotonic

Accepted by Council of Pharmacy & Chemistry of the A. M. A. (N. N. R.)

Write for Sample and Literature to

BETHLEHEM LABORATORIES, Inc.
BETHLEHEM, PA.

Manufactured by
General Laboratories
Madison, Wis.

For
Bethlehem Laboratories, Inc.
Bethlehem, Pa.

CONTENTS

ORIGINAL ARTICLES

Notes on the Diagnosis of Bronchopneumonia and its Complications . 1
By Nellis B. Foster, M.D., Assistant Professor of Medicine, Cornell Medical College, First Division, The New York Hospital.

Experimental Studies in Diabetes: Series II. The Internal Pancreatic Function in Relation to Body Mass and Metabolism. II. Changes in Assimilation by Alterations of Body Mass 16
By Frederick M. Allen, M.D., New York.

Benzyl Benzoate in Pediatric Practice 32
By John Ruhräh, M.D., Baltimore, Maryland.

Studies in the Physiology of the Liver: I. Technic and General Effects of Removal 37
By F. C. Mann, M.D., Associate Professor of Experimental Surgery and Pathology, The Mayo Foundation, Rochester, Minn.

Alimentary Hypersecretion; Gastric Hypersecretion; Gastrochronorrhea 43
By Burrill B. Crohn, M.D., and Joseph Reiss, M.D., New York.

Observations upon the Treatment of the Chronic Intestinal Invalid . . 63
By John Bryant, M.D., Boston, Mass.

On the Etiology of Typhus Fever 78
By Edwin W. Schultz, M.D., Stanford University, California.

Acute Epidemic Encephalitis 91
By Charles H. Miner, M.D., and Stanley L. Freeman, M.D., Wilkes-Barre, Pa.

Recurrent Type I Pneumonia: Serum Treatment of Two Attacks One Month Apart 103
By Henry M. Thomas, Jr., M.D., Boston, Mass.

(Contents continued on page 12)

FOR **DIABETICS**

CELLU FLOUR

A non-nutritive flour for filling out reduced diets

27 oz. Bags $2.50 postpaid

Larger quantities at lower rates—Recipes furnished

DIETETIC CELLULOSE COMPANY, 2557 W. Chicago Ave., Chicago, Ill.

The New METABOLIMETER

Designed for bedside studies in

BASAL METABOLISM

"The proof of accuracy of a basal metabolism method is (1) *to determine how closely it will duplicate its own readings, when taken within the same hour, on the same subject, by the same technician, and* (2) *to determine from a large series of individuals, how its readings on normal subjects compare with the accepted average rates of normal persons."*

A duplicate of the model devised in the Department of Pathology, University of Illinois College of Medicine, Chicago, by Horry M. Jones, Ph.D., and reported in the Journal A. M. A. of August 21, 1920.

At present you may have in mind some method or apparatus which everyone has told you is the most accurate method now in use. And you believe it, either because everyone says that it is, or because some well-known institution publicly sanctions its use. Did it ever occur to you how simple it is to reduce this reputed accuracy to a real basis of truth? The scheme is simply to require the apparatus you have in mind to be used, in say about four consecutive tests, on the same person, during the same hour, by the same technician. Then check up the gas analyses and calculations, yourself, to the end-result. Take nothing for granted. Use the research method. You have a right to be shown the limitations of any method. And most important of all, do it before, not after, you have adopted the apparatus as part of your hospital or research equipment. Imagine yourself installing an expensive, cumbersome outfit, solely on its reputed accuracy and then discovering that it requires sixty times as much time and expense as another simpler method which you can easily and quickly demonstrate is equally as accurate.

We appreciate this critical, discriminating attitude. Why? Because, from whatever angle you investigate the methods now available for this purpose—whether from the standpoint of accuracy, of simplicity, of comfort to the patient, of price, of portability, of freedom from overhead expense for an extra technician for gas analysis and calculation, the more thoroughly you investigate, the more surely you will come eventually to accept the METABOLIMETER as the instrument most suitable for accurate work in research and practicability in clinical uses in basal metabolism studies.

Write for a list of leading institutions and internists who depend absolutely on its accuracy in the diagnosis of their borderline cases

MIDDLEWEST LABORATORIES CO., 1655 N. Sawyer Ave., CHICAGO, ILL.

Makers of Scientific Apparatus

The Colloidal Gold Curve in Epidemic Encephalitis: A Preliminary Note 109
By THOMAS K. DAVIS, M.D., and WALTER M. KRAUS, M.D., New York.

Carcinoma of the Supra-ampullary Portion of the Duodenum . . . 111
By N. B. HERMAN, M.D and WILLIAM C. VON GLAHN, M.D., Baltimore, Md.

Etiology of Acne Rosacea Through a Viscero-Neurologic Mechanism . 120
By FRANK PORTER MILLER, M.D., Los Angeles, Calif.

REVIEWS

Diseases of Children. By John Lovett Morse, M.D. 125
An Atlas of the Primary and Cutaneous Lesions of Acquired Syphilis in the Male. By Charles F. White, M.B., Major, R.A.M.C., and W. Herbert Brown, M.D., late Captain, R.A.M.C. 125
Index of Symptoms. By Ralph Winnington Leftwich, M.D. 126
Eating to Live Long. By William Henry Porter, M.D. 127
International Clinics. By H. R. M. Landis, M.D. 127
The Duodenal Tube and its Possibilities. By Max Einhorn, M.D. . 127
Surgical Clinics of Chicago 128
Mental Deficiency (Amentia). By A. F. Tredgold, M.D., F.R.S. (Edin.) 128
Physical Basis of Heredity. By Thomas H. Morgan 129
The Nature of Animal Light. By E. N. Harvey, Ph.D. 130
Das Geschlectsleben der Naturvoelker. By H. Fehlinger 130
Exophthalmic Goiter and its Non-surgical Treatment. By Israel Bram, M.D. 131
Marine Hygiene and Sanitation. By Gilbert E. Brooke, M.A. (Cantab.), L.R.C.P. (Edin.), D.P.H., F.R.G.S. 132

(*Contents continued on page 14*)

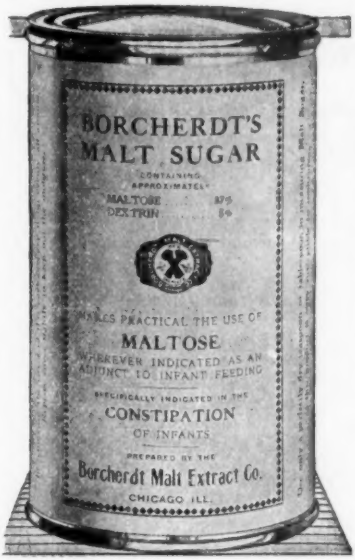
Trade Mark Registered.
Gluten Flour
40% GLUTEN
Guaranteed to comply in all respects to standard requirements of U. S. Dept. of Agriculture.
Manufactured by
FARWELL & RHINES
Watertown, N. Y.

SALIPYRIN
"RIEDEL"

"THIS compound possesses the properties of both antipyrine and salicylic acid and combines the analgesic power of the one with the antirheumatic action of the other. It has been used with good results in sciatica, rheumatic fever, chronic rheumatism, influenza, pleurisy, dysmenorrhea, etc."—(*New and Nonofficial Remedies, 1920, American Medical Association.*)

Riedel & Co., Inc.
Bush Terminal Bldg. No. 5, Brooklyn, New York City

87.4% PURE MALTOSE
For Infant Feeding



Borcherdt's Malt Sugar may be obtained at most druggists

Borcherdt's Malt Sugar

makes practical the use of Maltose in any proportion desired for infant feeding. As a carbohydrate addition to the infant's diet it offers these advantages.

ASSIMILABILITY—Maltose being the ultimate end-product of malt diastase action, requires little if any digestion.

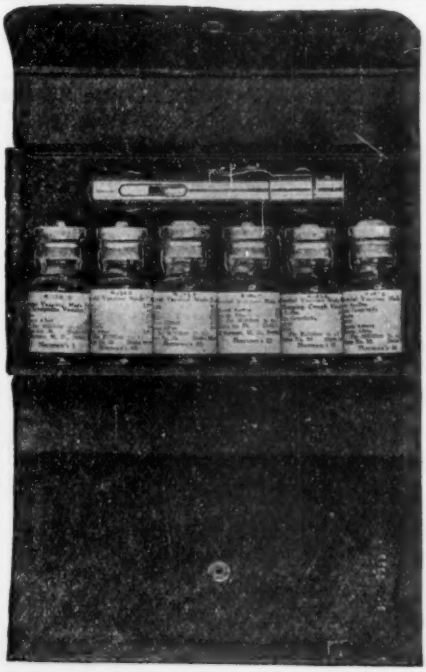
TOLERANCE—It places a minimum tax on the digestive apparatus, hence its ready tolerance by weak, malnourished infants as well as by those who are in normal tone.

CORRECTION OF CONSTIPATION—Maltose invariably increases the frequency of the stools. With the high percentage of Maltose furnished by Borcherdt's Malt Sugar, the diet may be quickly and definitely adjusted to overcome constipation.

Descriptive Literature, Samples and Analysis Sent on Request

Borcherdt Malt Extract Company

217 North Lincoln Street **Chicago**



SHERMAN'S VACCINE CASE

The best immunizing response in Pneumonia is obtained during the first twenty-four hours after the initial chill. Every hour being vitally important, successful immunologists make inoculations in Respiratory Infections at their first call.

Be prepared; carry an assortment of Sherman's Polyvalent Vaccines and self-sterilizing syringe in this convenient case.

Your dealer will be pleased to supply you.

G. H. Sherman, M. D.
DETROIT - - MICHIGAN

Largest Producer of Stock and Autogenous Vaccines

CONTENTS—(*Continued*)

PROGRESS OF MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF

W. S. THAYER, M.D., ROGER S. MORRIS, M.D.,

AND

THOMAS ORDWAY, M.D.

A Study of the Correlation of the Basal Metabolism and Pulse-rate in Patients with Hyperthyroidism 133
Observations upon Flutter and Fibrillation 133
Mononuclear Leukocytosis in Reaction to Acute Infections (Infectious Mononucleosis) 134
The Relationship of Smallpox and Alastrim 134
Acute Respiratory Infections at the Boston City Hospital 135

SURGERY

UNDER THE CHARGE OF

T. TURNER THOMAS, M.D.

The Management of Fractures of the Femur 135
Etiology, Pathology and Clinical Features of Benign Exostoses . . . 136
The Radical Treatment of X-ray Burns 136
Sarcoma of the Clavicle 137
Gall-bladder Disease 137
Distribution of Adenomyomas Containing Uterine Mucosa 138
Intussusception Resulting from Benign Tumor of the Intestine . . . 138
Tuberculosis of the Breast 138

(*Contents continued on page 16*)

DIGITALIS MEDICATION ORALLY-INTRAVENOUSLY OR INTRAMUSCULARLY

is obtained in full degree, promptly and potently

by the use of

DIGALEN

"ROCHE"

From druggists everywhere in

VIALS AMPULS TABLETS

and HYPODERMIC TABLETS.

Free Trial Supply and Literature from THE HOFFMANN-LA ROCHE CHEMICAL WORKS ~ NEW YORK

BACILLUS ACIDOPHILUS

Bacid

PREPARATIONS

TABLETS—CAPSULES—LIQUID CULTURES

INTRODUCE

the *Bacillus Acidophilus* which is an organism *of* high acid producing (antiputrefactive) qualities whose

Normal Habitat is the Human Intestine

To ensure a sufficiency *of* this natural defensive organism, when depletion or extinction occurs from any cause whatever, we now offer this

Bacillus Acidophilus in Bacid Preparations as a **new therapeutic agent**

LITERATURE—BIBLIOGRAPHY—ON REQUEST

Guaranteed and Manufactured ONLY by

The Arlington Chemical Company

YONKERS, N. Y.

Standard Product in Heart Cases

Digitan introduced as

Digipuratum

Physiologically Standardized Digitannoids

This product, first introduced as Digipuratum, is manufactured under license from the Federal Trade Commission and carefully standardized according to the original tests

RAPID AND RELIABLE IN ACTION. UNIFORM IN STRENGTH

Supplied in Powder and 1½ grain Tablets

1½ grains powder or 1 tablet Digitan equal to 1½ grains strongly active digitalis leaves = 8 frog units

MERCK & CO. - - NEW YORK and ST. LOUIS

THERAPEUTICS

UNDER THE CHARGE OF

SAMUEL W. LAMBERT, M.D., AND CHARLES C. LIEB, M.D.

The Digestion of the Tannin Compounds Used as Intestinal Astringents by Artificial Digestive Mixtures. Synthetic Drugs, III 139
The Use of Arsphenamin in Non-syphilitic Diseases 140

PEDIATRICS

UNDER THE CHARGE OF

THOMPSON S. WESTCOTT, M.D., AND ALVIN E. SIEGEL, M.D.

Further Progress in the Study of the Relative Efficiency of the Different Mercurial Preparations 140
A Study of Streptococci Obtained from the Mouth in Cases of Chorea . 141
Spasmophilia and Vitamins 141
Three Pertinent Questions on Maternal Feeding 142
The Superior Longitudinal Route 142
Social and Medical Aspects of Childhood Delinquency 142
A Note on Vitamines in Relation to Scurvy and Rickets 143
The Diagnosis and Treatment of Hydrocephalus Resulting from Stricture of the Aqueduct of Sylvius. 143

OBSTETRICS

UNDER THE CHARGE OF

EDWARD P. DAVIS, A.M., M.D.

Treatment of the Severe Vomiting of Early Pregnancy 144

(*Contents continued on page 18*)

ORIGINATION BEGETS IMITATION

Electrically Lighted Surgical Instruments

BE SURE OF OUR EXACT NAME

Twenty years in the manufacture of electrically lighted surgical instruments, if it has not brought perfection in instrument construction, at least has kept the Electro Surgical Instrument Company abreast of the advances made by leading specialists of the medical and surgical profession.

So it is that instruments stamped "E. S. I. Co." speak of the accomplishments of the noted men whose suggestions are embodied in their construction and a service of maintenance possible only in instruments of our manufacture.

Users of instruments stamped "E. S. I. Co."
are certain sharers in this service.

Illustrated Catalogue Sent Upon Request

ELECTRO SURGICAL INSTRUMENT CO.

ROCHESTER, N.Y.

New Victor Fulguration Coil

(Portable)

The successful use of the high frequency current in the treatment of bladder tumors for a number of years, has led to an urgent demand for specialized apparatus for this work.

Victor engineers have given close study to the requirements during this period and in this most recent design, the Victor Fulguration Coil, is presented the closest approach to the ideal for this work.

The first requisite for high frequency fulguration is a current void of any faradic sensation and which is under a finely graduated control. In these respects this outfit far excells any construction yet offered.

An exclusive feature in this apparatus is the fulguration meter, which indicates the relative intensity of heat produced at the electrode. This makes it possible to duplicate technique, by simply recording the meter reading and the settings of the inductor and condenser switches. The advantages of this exclusive feature are all-important to every operator.

This outfit is also admirably adapted to superficial fulguration, as well as treatment work with vacuum or non-vacuum electrodes. There is a fine graduation over the entire ranges of both mild and strong currents.

Although a highly refined apparatus, it is simple to operate and of the desired durability. It is portable, weighing but 10 pounds. The various parts are so mounted that the condenser, inductance coil, etc., may be disconnected and removed independently without disturbing other parts of the outfit.

Descriptive Bulletin Sent on Request

VICTOR X-RAY CORPORATION

General Offices and Factory:

Jackson Boulevard and Robey Street
CHICAGO

Sales Offices and Service Stations in all principal cities

GYNECOLOGY

UNDER THE CHARGE OF

JOHN G. CLARK, M.D., AND FRANK B. BLOCK, M.D.

Conservatism in Pelvic Inflammatory Disease 148
Differential Diagnosis of Tumors by Means of Roentgen Ray 148
Operation for Pruritus of Anus and Vulva 149
Treatment of Inoperable Cancer with Selenium 150
Combined X-ray and Radium Treatment of Uterine Carcinoma . . . 151

PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

OSKAR KLOTZ, M.D., C.M.

The Action of Benzol 151
Effect of Intrabronchial Insufflation of Acid 152
Histological Changes of the Different Types of Carcinoma after Exposure to Radium Rays 153

HYGIENE AND PUBLIC HEALTH

UNDER THE CHARGE OF

MILTON J. ROSENAU, M.D., AND GEORGE W. McCOY, M.D.

Notes on Typhus 154
Influence of Smallpox and Vaccination on Pulmonary Tuberculosis . . 156

INDEX TO ADVERTISERS

A WORD TO OUR SUBSCRIBERS—these advertising pages are *clean;* no medical journal sets a higher standard. Only ethical products, and of the highest quality, can gain admittance to these columns. We believe that you can place absolute confidence, as do we, in the firms listed below, all among the leaders in their fields. In writing them, mentioning THE JOURNAL would be appreciated.

Apparatus and Instruments
(Bacteriological, Diagnostic, Sterilizers, etc.)

Wilmot Castle Co. 7
Electro Surgical Instr. Co. 16
Chas. F. Hindle 2
Middlewest Laboratories Co. 11
Precision Ther. and Instr. Co. 25
Rieker Instr. Co. 6
Sanborn Co. 8
Spencer Lens Co. 5
Arthur H. Thomas Co. . . 3

Biologicals, Drugs, Pharmaceutical Supplies, etc.

Arlington Chemical Co. . . 15
Armour & Co. 21
Bethlehem Laboratories, Inc. 9
Ciba Co. . . . . 4th Cover
Dermatological Research Laboratories 21
Diarsenol Co., Inc. 24
Fairchild Bros. & Foster . . 5
Hoffmann-LaRoche Chemical Works 14
Intra Products Co. 30
Lederle Antitoxin Laboratories. . . . . 2d Cover
Eli Lilly & Co. 1
Merck & Co. 15
H. A. Metz Laboratories, Inc. 29
Parke, Davis & Co. 28
Riedel & Co., Inc. 12
Schering & Glatz, Inc. . . . 19
Dr. G. H. Sherman 13
E. R. Squibb & Sons. 20
United Synthetic Chemical Corporation 31
Winthrop Chemical Co., Inc. 30

Foods, etc.

Borcherdt Malt Extract Co. 13
Dietetic Cellulose Co. 10
Farwell & Rhines 12
Health Food Co. 7
Horlick's Malted Milk Co. 31
Lister Bros., Inc. 19
Mellin's Food Co. . . . 4th Cover
Quaker Oats Co. 31

Health Resorts

Battle Creek Sanitarium 35
Glen Springs 26
The Homestead (Hot Springs, Va.) 6

Radium

W. L. Cummings Chem. Co. 25
Radio Chemical Corp. . . . 4
Radium Co. of Colorado, Inc. 26

X-Ray Apparatus, Tubes, etc.

Victor *X*-Ray Corp. 17
Waite & Bartlett Mfg. Co. 22 23

Miscellaneous

American Institute of Medicine. . . . . 3d Cover
The Fleischmann Co. 27
Kalak Water Co. 35
Lea & Febiger 32 34
Charles T. Powner Co. . . . 6
Standard Oil Co. of N. J. 36

Atophan

Again, with unfailing regularity, paying its annual visit—Influenza
(La Grippe)

And Influenza time is truly ATOPHAN time.

Here ATOPHAN can fully unfold its superior pain and inflammation relieving properties.

One, or two, tablets (7½ to 15 grains) two or three times per day, immediately after meals, readily alleviate respiratory congestion, headache, pain and stiffness of limbs and back.

And remember, ATOPHAN does it without heart depression, constipation or kidney irritation.

In high and persistent fever, let a few doses of some more active antipyretic round out the good work of ATOPHAN.

U. S. A.-Made and Available Everywhere

SAMPLE AND LITERATURE FROM

SCHERING & GLATZ, Inc. - 150 Maiden Lane, NEW YORK

STARCH-FREE DIABETIC FOODS

BREAD, MUFFINS, BISCUITS, COOKIES, ETC. EASILY MADE IN ANY HOME

ANALYSIS

Moisture	10.66
Ash	1.63
Fat	0.67
Protein	69.95
Starch	0.00
Sugar	0.00
Leavening & Flavoring	17.09

NO PURINS
NO GLUTEN

LISTERS
PREPARED CASEIN
DIABETIC
FLOUR

This Flour is put up in boxes, enough in each for one loaf of bread or six muffins. A case of 30 of these boxes—(a month's supply, price $4.85.)

Self-Rising. Accepted by The Council

LISTER BROTHERS, Inc. Office, 405 Lexington Avenue, New York City

SQUIBB

Research & Biological Laboratories

THYROXIN SQUIBB

The chemically pure, physiologically active constituent of the thyroid gland, introduced by Kendall and made by E. R. SQUIBB & SONS under license of the University of Minnesota. Possesses all the activity of desiccated thyroid and offers the advantage of accuracy in dosage and therapeutic effect. Marketed in tablets of 1/320, 1/160, 1/80, and 1/32 grain each for administration by mouth. Crystalline Thyroxin for intravenous use is supplied in vials of 10 milligrammes to 100 milligrammes.

NOW READY FOR DISTRIBUTION.

SEASONABLE BIOLOGICALS

ANTIPNEUMOCOCCIC SERUM SQUIBB
Type I

DIPHTHERIA ANTITOXIN SQUIBB
(Small in Bulk—Low in Solids)

LEUCOCYTE EXTRACT SQUIBB
(An adjunct to Serum and Vaccine Therapy)

SMALLPOX VACCINE SQUIBB
(In Capillary Tubes)

THROMBOPLASTIN SQUIBB
(Physiologic Hemostatic)
(Local and Hypodermic)

For almost three-quarters of a century this seal has been justly accepted as a guaranty of trustworthiness.

E·R·SQUIBB & SONS, NEW YORK
MANUFACTURING CHEMISTS TO THE MEDICAL PROFESSION SINCE 1858

THE

AMERICAN JOURNAL

OF THE MEDICAL SCIENCES

JANUARY, 1921

ORIGINAL ARTICLES.

NOTES ON THE DIAGNOSIS OF BRONCHOPNEUMONIA AND ITS COMPLICATIONS.

By Nellis B. Foster, M.D.,

ASSISTANT PROFESSOR OF MEDICINE, CORNELL MEDICAL COLLEGE, FIRST DIVISION, THE NEW YORK HOSPITAL.

Reference to any standard text will lead to the inference that primary bronchopneumonia in adults is not a common disease. That it is the usual type of pneumonia in children is accepted as well as that "terminal pneumonias" are commonly of the catarrhal variety. But that bronchopneumonia is at all confined to the extremes of life, childhood and old age is, I believe, incorrect. It will be the purpose of this paper to present evidence indicating the frequency of this type of pneumonia, to discuss the several pathologic and clinical pictures that may be grouped under the generic heading of broncho- or lobular pneumonia and their more serious complications.

In assuming a position which may seem at variance with usual conceptions of incidence, an explanation is appropriate as to why bronchopneumonia may at times escape detection and be passed over as simple bronchitis. The explanation is simple: (1) the physical signs are frequently transitory, and (2) the patient may not seem sick—that is, sick enough to excite careful examination. Pneumonia is closely associated in our mind with a group of rather definite symptoms and, in the absence of these, the examination made is liable to be either perfunctory or entirely omitted. The

fleeting, evanescent character of the physical signs can hardly be appreciated unless one has experience in ward-teaching. Time and again the signs found at morning rounds were gone in the area marked when the patient was shown at the afternoon clinic, and this explains the development of hospital routine regarding radiograms. The instructor was at times in sore need of demonstrable evidence. From this the logical step was natural of radiographing many cases of "simple bronchitis" in which no sign of consolidation had at the time been noted. The results of these examinations were illuminating; at first in revealing what we did not detect and later in confirming a suspected lesion. What interpretation is to be placed upon a record of this sort? A healthy man of twenty-six years was admitted to hospital January 20 complaining of a cold which he attributed to a wetting two days before. He had felt a little feverish the night before admission, but not sick. He said he did not feel sick enough to be in bed, but a "bit fagged." His temperature was 101°, respiration 22, pulse 90. Examination showed only rales scattered throughout both lungs: No dulness; no change in breath sounds; pectoriloquy absent. A radiogram taken on the day of admission showed an area of density, the size of an egg, just above the heart shadow in the left chest an inch from the hilus of the lung. On January 22 the shadow was still present: the patient had improved and the fever had gone. A final plate, taken on January 28, showed only a slight residual clouding in the area mentioned. At no time had there been physical signs other than those of a bronchitis (rales): at no time had the patient seemed or felt really ill. A repetition of this experience over and over gave ground for the hospital dictum—"bronchitis is rarer than a bronchopneumonia"—and this apparently extravagant assertion accords with my experience in private practice. That the patient may not feel sick, nor look more so than one does with a cold, that the temperature is but slightly elevated is sufficient explanation for neglect of searching examination. History records the "incidence of most diseases has increased with their recognition."

Not only is bronchopneumonia a very common disease in hospital practice, but the incidence will be found high among healthy young men in colleges, as I have had opportunity to observe, and it was one of the common diseases in the cantonments at periods when no epidemic prevailed. Furthermore the nature of disorders which are traced back to "colds" would be best explained by pneumonia, and these disorders are not few.

Bronchopneumonia, as the name indicates, is very often purely an extension of an infection from the smaller bronchi to contiguous pulmonary tissue. The disease seems to have been first described by Bartels, although Laennec mentioned the scattered areas of infiltration found in some cases of catarrhal bronchitis. Common usage has made the terms bronchopneumonia and lobular pneu-

3104C1
19 Jy 44

monia synonymous. Some pathologists, however, draw distinctions which are not generally accepted, and until the processes are better understood in their mode of production, are useless. The morphology of broncho- or lobular pneumonia is determined largely by the type of infection, and, to some extent at least, by whether the infection enters through the respiratory tract or the blood stream. The more general aspects which characterize the pathology of lobular pneumonia have a common basis in all types. On section of the diseased lung the fresh surface has a notably "patchy" character; certain areas are raised, and at the center of these areas may usually be found the bronchi, seen as grayish spots from which pus may be expressed. The involved areas may be numerous and discrete, or they may coalesce into large consolidations; even when a considerable portion of a lobe is involved in the consolidation the picture does not often resemble lobar pneumonia. The cut surface is less granular and there is not liable to be much fibrin or leukocytic detritus as with lobar pneumonia. Between the areas of consolidation atelectasis occurs, due to stoppage of the bronchioles, with resorption of air and resulting collapse of the alveoli. In its earliest stage scattered areas of bronchopneumonia may appear as numerous discrete, minute tubercles, shotty to feel, gray or brownish in color, and surrounded by areas of reddish atelectatic tissue. When the lung presents this picture at necropsy it may be mistaken for miliary tuberculosis (and the radiogram is equally misleading). A later stage represents the enlargement of these small areas with coalescence. Thus a whole lobe may be involved, but the patchy character of the cut surface is usually preserved: massive, confluent, lobular pneumonia. Minor differences are determined, it seems, by the nature of infection and the resistance of the individual. The salient fact in this pathologic process is that it takes origin in a bronchiole. Following a bronchus into a diseased portion of the lung by dissection discloses that the consolidation is terminal or lateral to a bronchus.

Bronchopneumonia is usually thought of as a complication of typhoid fever ("typhoid pneumonia"), measles, diphtheria and occasionally of scarlet fever. The causative infecting agents are numerous. With the primary type of bronchopneumonia the pneumococcus is often found, even Type I pneumococci has been repeatedly isolated from sputum of some of my cases. Pneumococcus type IV is more common, while probably a majority of the cases of lobular pneumonia are due to streptococci, either as a primary infection or mixed with some other organism. The role of the streptococcus in these processes is by no means clear, in spite of the fact that it has been repeatedly isolated from both the sputum and from the lung tissues of cases dead of pneumonia. The reason for some doubt rests in the conception that the streptococcus infections are prone to be secondary. Weichselbaum illustrated the point

years ago with reference to empyema, which may, in the initial stage, show only pneumococci in the pus; later the pneumococci are overgrown and disappear and the pus contains only streptococci.[1] For example, measles pneumonia, a typical secondary infection, is predominantly a streptococcus pneumonia. The primary invader may be an organism of relatively slight virulence, but, given a predisposition, the tissues are made vulnerable by this trivial infection and the streptococcus finds a suitable environment for growth. Coryza is often due apparently to an invasion of the Micrococcus catarrhalis, an organism of weak pathogenicity, a secondary infection with streptococcus takes place and pneumonia develops. This expresses the present conception of the mode of origin of a group of diseases due to streptococcus infections, and it is the sole scientific basis for the face mask so much used in military hospitals; protecting an individual susceptible on account of some slight infection from inhaling streptococci thrown out by persons already infected. The practical difficulty in this prophylaxis is that so many healthy persons harbor Streptococcus hemolyticus in the throat. Mathers found hemolytic streptococci in the throats of 70 per cent. of a healthy organization at Camp Meade. These questions have not only scientific interest, but are in the front rank of practical considerations when diseases such as measles are to be cared for. For some time pediatrists have recognized that the incidence of pneumonia complicating measles is higher in even very good hospitals than among children cared for in their homes, and an impression growing toward conviction is notable that, under certain conditions, pneumonia may spread as a contagion in measles wards. The factor that is outstanding in my experience in determining the incidence of pneumonia complicating measles is the season of the year; in the cold months there has been a higher percentage of pneumonia than occurred in the warm parts of the year, and this has been true even with the most rigid methods of individual isolation. Is the body's resistance so generally lowered by cold weather?

The factors which predispose to pneumonia may be classed under two headings: those which lower the vitality of the individual and those which lower the resistance of the pulmonary tissues. Under the first heading would come not only the diseases generally recognized as terminating with bronchopneumonia, chronic and cachectic diseases and certain acute infections, such as the exanthemata, but also those conditions which suddenly reduce immunity, and here fatigue takes first place. With sound, healthy individuals no factor seems to be so potent in lowering resistance to infection as is fatigue. Probably this is in some degree true of all infections; it can hardly

[1] The advent of filtrable viruses further complicates the question and postpones definite decision. In relation to this question, see the communication of Roux to the Académie des Sciences, at the November meeting, 1918, dealing with pathogeneses of influenza.

be controverted in relation to pneumonia. Other factors of significance are hunger and chilling from exposure. All of these factors more or less enter into consideration with all types of pneumonia, lobar as well as lobular. In one case the invasion is prompt and sudden and lobar pneumonia develops; in another, more insidious or perhaps in the beginning milder, a "simple cold" with bronchopneumonia later.

Of the factors which lower the resistance of pulmonary tissues mild and even trivial infections are paramount: trivial infections are ignored. It was notable in all cantonments that those organizations that sent their cases of minor sickness to hospital had the lowest incidence of pneumonia. The significance is clear: with a mild bronchitis a bed is the best prophylactic against pneumonia. The resistance of pulmonary tissues to infection is also lowered by mechanical and chemical irritation; dust, especially sand, gases and smoke, ether and chloroform. Postoperative pneumonia is due evidently to several factors: the technical skill of the operator, the purity of the ether and skill of administration and the care of the patient during the period while he is recovering from the anesthetic, especially respecting warmth. In several clinics, where opportunity has come to me to study many cases of pneumonia following operation, I have not been able to trace the cause nearer than outlined above. The question is important and deserves more careful study than has been given to it.

In *resume*, it may be briefly stated that any circumstance which lowers the vitality of the organism as a whole, or by irritation injures the pulmonary tissues, locally, predisposes to pneumonia. The invader is always at hand and the invasion depends upon the host.

Symptoms. The clinical picture of bronchopneumonia is most variable. At one extreme is the case with signs and no symptoms other than fever, at the other extreme is a clinical picture of the severest form of pneumonia. In truth, there are cases with marked symptoms and no corresponding signs, and others with slight symptoms and clearly defined signs. The mild cases offer some difficulty in diagnosis and are often overlooked, although deserving attention on account of the frequent sequelæ. It so often happens that the patient seeks help only on account of an annoying cough. With scarcely any pyrexia the tendency is natural to dismiss the case as one of acute bronchitis requiring no thorough examination of the lungs. Allowed up and about, perhaps at work, the patient's condition becomes serious before its nature is recognized. I have known this to occur not infrequently. The patient then takes to his bed only when exhausted or in collapse. With pneumonia little enough can be done for the patient other than securing him rest and protection of his vitality, and this should not be delayed.

Occasionally the period of active infection is passed before the

patient consults a physician. A number of cases belonging in this category have been encountered where relief was sought from a persistent cough following a "hard cold," and examination disclosed an area of consolidation, but no fever or other sign or symptom. Delayed resolution of this sort may be, and often is, mistaken for a tuberculous consolidation. A young physician consulted me for a confirmation of the diagnosis of pulmonary tuberculosis made by a specialist. The patient had had a severe bronchitis some two weeks before but had kept at work in spite of fever. The physical signs were confined to an area in the upper portion of the left lower lobe —a consolidation a couple of inches in diameter. This spot slowly resolved in the course of a month. With vigorous, sthenic individuals, bronchopneumonia is, I am convinced, occasionally experienced as a "bronchial cold," and with no more results.

The onset is occasionally sudden, resembling in this respect lobar pneumonia; more often there is a gradual development, commencing as a "cold," with slight cough, becoming more severe until the patient is driven to his bed. Pleural involvement occurs late in contrast to lobar pneumonia. In the early period of the disease the temperature may not be above 101° F., the pulse but slightly increased and the respirations not accelerated. Drenching sweats are common; cough is annoying and exhausting. The sputum varies; there may be considerable amounts of mucopurulent material, with no obvious admixture of blood—with other cases the sputum is greenish pus, or, again, it resembles brick dust in color. When the infection is severe, dyspnea is often a striking symptom, and this, with the marked cyanosis, recalls the old name of the disease "suffocative catarrh." With many cases death appears to result from asphyxia rather than from a wearing out of the myocardium, as in lobar pneumonia.

The nervous symptoms are most striking. Delirium is common, not of the low, muttering type, but violent, often maniacal. A peculiar typhoid state with delirium, marked tremor and coma vigil is occasionally noted. Many patients complain of excruciating headache, and with this signs of meningismus are frequent. Relief is often prompt, following lumbar puncture and the removal of a half ounce of fluid. Headache with a stiff neck and a suggestive Kernig sign is an indication for lumbar puncture. The fluid in these conditions is under considerably increased pressure—the first half-ounce running so fast the drops cannot be counted. I have gained the impression that with some of these cases not only does the headache abate, but respiration is improved by relieving the intracranial pressure.

With severe bronchopneumonia the picture at times presented by the patient when the disease is at its height differs in many respects from lobar pneumonia. The deep, livid cyanosis arrests attention. The picture of suffocation with an excited, alert mental

state; the sweating; cold, clammy extremities in spite of a strong, regular pulse—a clinical picture not readily overlooked.

A type of pneumonia called interstitial is seldom recognized clinically, except by inference. The early symptoms suggest the onset of lobar pneumonia. Examination of the patient discloses signs of fluid in the pleural cavity. These are the cases of primary empyema (so called). The characteristic feature is the rapid formation of the pus. A patient having only symptoms of an infection may, within six or eight hours, develop symptoms of intrathoracic pressure, with signs indicating a pleural cavity full of fluid. To one who has not watched such cases and seen the pus return after aspiration and fill a cavity overnight the peculiar feature of this infection is scarcely creditable. Interstitial pneumonia received some attention in cantonment hospitals during last winter. Kaufmann's[2] classical description covers the essential features of the pathology.

Diagnosis. The diagnosis of bronchopneumonia cannot invariable be arrived at from the physical signs alone. Those somewhat unusual cases of multiple, discrete foci give none of the typical signs of consolidation, and these could not be expected when the foci are no larger than peas. The picture presented by the radiogram is misleading to the unwary and is not infrequently regarded as miliary tuberculosis, which, indeed, it may resemble post mortem. The signs in these cases are those we customarily associate with bronchitis. There is, however, something more than rales to be heard; a variability in the intensity of the breath sounds in contiguous areas is peculiar and arrests attention if one be on the lookout for this phenomenon. However, in some cases the diagnosis must be inferred, the temperature being too persistent and an increased respiratory rate speaking against bronchitis. When possible to procure one, stereoscopic radiograms may aid in confirming the diagnosis.

Even relatively small areas of consolidation are detectable by a skilled technic. Unless the area involved be near the costal pleura, however, impairment of resonance and frank change in breath sounds will not be notable. The change in the character of the signs over suspected spots at different examinations is in itself significant. The fleeting and migratory character of the consolidations in lobular pneumonia is peculiar to the disease. The earliest definite sign, and the one of most help when other signs are equivocal, is the change in the whispered voice which is transmitted to the ear with an abnormal clearness and with a slight nasal quality. Transmission of the whispered voice is a helpful sign in the recognition of changes of density in the lung substance and is often the earliest sign in all types of pneumonia. Because this sign is so frequently neglected some amplification is appropriate. A confusion exists in the minds

[2] Speziellen Path. Anat., 1911, 261.

of many concerning the significance of variations in the transmission of sound vibrations, because the attention is given only to intensity or loudness of sound, whereas variations in quality of the sound or in its pitch are even more significant and the examiner must take pains to keep these several features entirely distinct. For example, sounds of low pitch are better transmitted to the chest wall through normal lung than are equally intense sounds of higher pitch. With a solid lung, on the other hand, vibrations of all pitch are equally well transmitted. In bronchopneumonia small areas of consolidated lung substance are surrounded by air-containing lung, and this latter appears to "dampen" some vibrations more than others; the overtones being least affected are transmitted to the chest wall. Another factor is the bone conduction of the spoken voice which enters as a confusing element in auscultation; this confusion is less

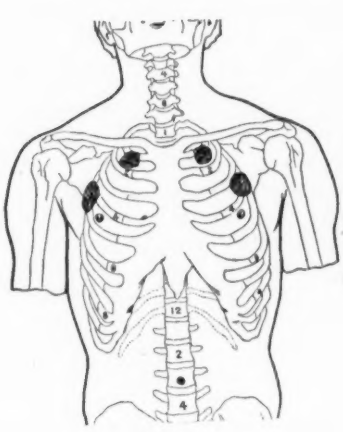


FIG. 1

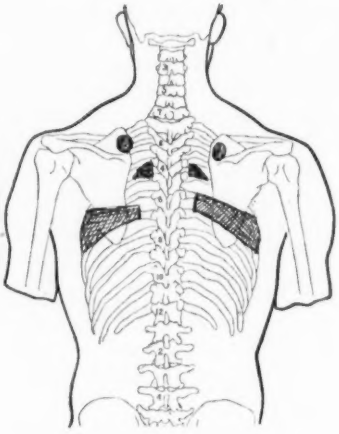


FIG. 2

pronounced or negligible in whispered pectoriloquy. Flint called attention to elevation of pitch as a sign of consolidation and the nonessential factor of mere intensity of sound.[3] It has repeatedly happened that whispered pectoriloquy was the only definite physical sign over small areas where consolidation was demonstrated by radiogram. Where the consolidation is of considerable size there is usually no difficulty in its recognition.

Bronchopneumonia, alike with lobar pneumonia, shows a predilection for the lower lobes and is noted most frequently in certain areas which are illustrated in the charts (Figs. 1 and 2). The mild cases, infections of low virulence, may not come under observation until

[3] See a clarifying analysis of these factors by Adams and Montgomery, Jour. Am. Med. Assn., 1919, lxxii, 987.

convalescence, and then the question of tuberculous infection is often uppermost. The site of the consolidation is of help in decision on this question, as tuberculous infections are not usually located in the bases of the lungs. The confusion of tuberculosis with delayed resolution of bronchopneumonia has been the subject of frequent remark by those especially interested in tuberculosis,[4] and it will be recalled that the mistake was made so often in the army that it became necessary to restrict the diagnosis of tuberculosis to those cases with tubercle bacilli in the sputum. Comment on this significant fact is hardly necessary.

Complications in lobular pneumonia, according to my case records, are more common than with lobar pneumonia. Except in young children, otitis media can hardly be overlooked, but empyema and pulmonary abscess very frequently escape recognition. Some experience outside of medical centers has convinced me that the so-called "septic pneumonia" of rural districts is usually empyema. Two erroneous notions are primarily responsible for the failures of recognition of empyema: (1) the idea that empyema is accompanied by a definite type of temperature curve, and (2) the idea that empyema gives rise to definite, characteristic physical signs. Both of these conceptions are narrow and misleading. The diurnal variation of temperature which is expected is so frequently absent that the type of fever is of little aid in diagnosis. While it may be true that with empyema following lobar pneumonia the temperature comes to normal in the majority of cases and then again becomes elevated, this fact is seldom applicable to the fever of empyema following lobular pneumonia. The accompanying charts (1 and 2) illustrate the diversity of febrile reactions. In some cases a sharp rise in the pulse-rate is more significant than the temperature curve.

Occasionally small pleural abscesses become so walled off that there is slight or no fever, the patient remaining an invalid for indefinite periods. In one case of this type the history pointed to an ambulatory pneumonia fourteen months before as the cause of the abscess.

The physical signs of empyema are so variable and departures from the text-book descriptions so frequent that it is necessary to hold broad and elastic conceptions and abandon the definite picture customarily held. Some cases undoubtedly show characteristic changes on examination, such as a dull or flat percussion note, impaired or absent vocal fremitus, with distant suppressed breath sounds approaching a bronchial type; but again it must be recognized that exceptions are exceedingly common.

Pleural abscesses tend to be sacculated and the surrounding lung tissue may be either consolidated in part or markedly emphysematous. The variations in these structural changes in the lung paren-

[4] Ash: Jour. Am. Med. Assn., January 2, 1915, lxiv, 11. McCrae and Funk, idem, July 19, 1919, lxxiii, 3.

chyma give origin to variations in physical signs; moreover, there seems to be a tendency for the focus of suppuration to take place first in a fissure between the lobes, with subsequent extension.

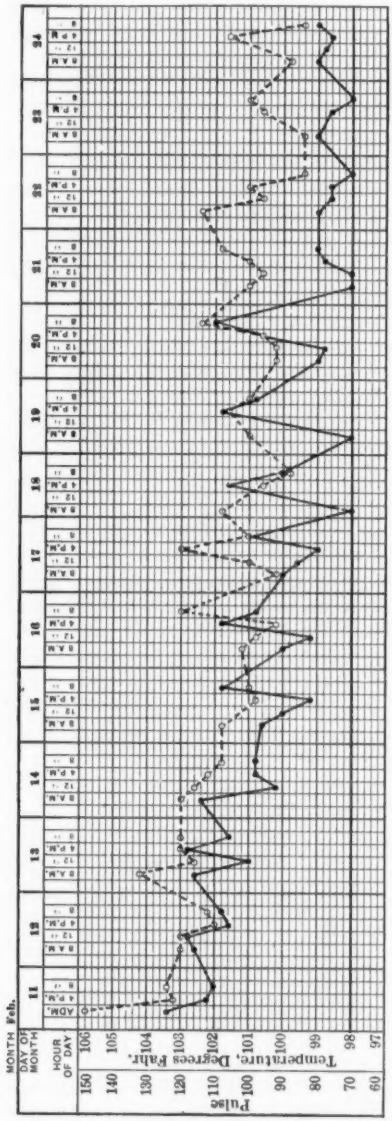


CHART I.—Typical bronchopneumonia. Empyema demonstrated on 19th.

When firm adhesions have been formed between the costal and parietal pleura there may be a thin lappet of air-containing lung between the ribs and pus. Postmortem examinations have revealed conditions of this sort and helped in an understanding of the marked variation in the peculiar physical signs. The fact should be emphasized that in many cases it is absolutely impossible to determine, by physical signs alone, whether the diseased condition in the lung is consolidation, fluid or both. The diagnosis, under these circumstances, can be determined only by exploratory puncture. Modified skodaic resonance in areas of the lung adjacent to collections of liquid has been to me of great assistance in diagnosis. The note elicited by percussion in the upper axillæ or over the lower portion

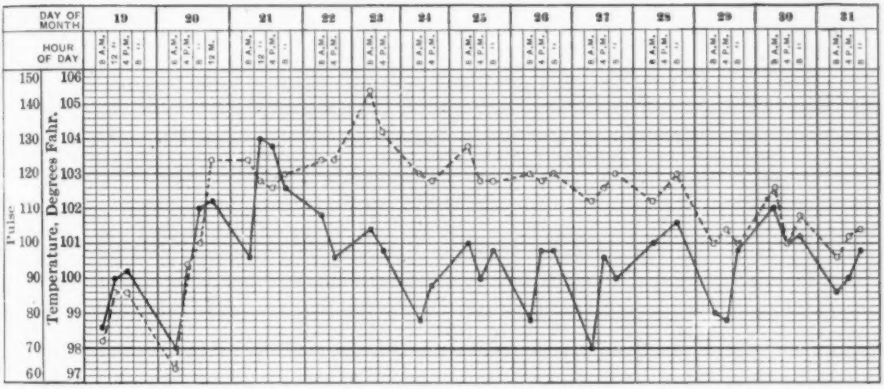


CHART II.—F. W., aged twenty-eight years. Case of Dr. Payne. Interstitial pneumonia (?). Empyema. On 20th, signs of slight bronchitis only; pain in the left chest. On 21st, at 10.30 A.M., careful examination failed to disclose suspected pneumonia; at 3.30 P.M. of same day, dulness, impaired fremitus and distant vesicular breath sounds over the left base posteriorly. Exploratory puncture. Pus. Infection due to Streptococcus hemolytic. Aspirations; operation on 30th.

of the upper lobe overlying or adjacent to fluid has a high-pitched tympanitic quality approaching the amphoric. This peculiar alteration in the percussion note I have only seldom detected in a like degree over areas of lung adjacent to consolidation. This skodaic resonance is so marked that in several instances examiners of skill have mistaken the underlying condition for cavity. To me this sign is more significant than impairment of resonance or even flatness in the percussion note over fluid. Fluid is not always detected, even when present, because the exploring needle is not introduced in the proper area and sometimes, indeed, the fluid cannot be found. An interesting example of this occurred in my service at Camp Meade Base Hospital. A patient developed, following pneumonia, typical signs of fluid in the pleural cavity. There was no dissent concerning

the diagnosis. The chest was needled by the ward surgeon with no success, by the assistant chiefs, the chief, and later by others on the staff. No interspace from spine to sternum in the suspected area

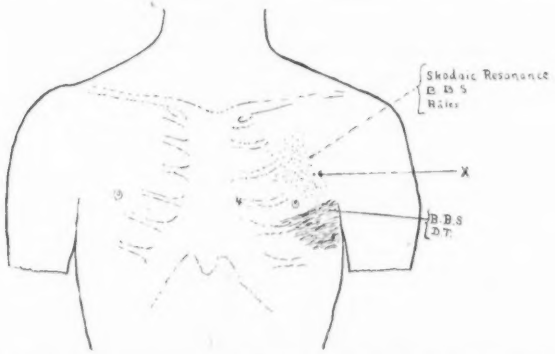


FIG. 3.—Atypical signs in empyema. Anterior view: Shading, impaired resonance to flatness; *A*, hyperresonant; *B*, skodaic resonance to amphoric; *D.T.*, "dry tap," *i. e.*, fluid not found; *X*, fluid determined by puncture; *B.B.S.*, bronchial breath sounds; *R*, rales, crepitant and subcrepitant.

escaped. The patient finally improved, the fever disappeared but the signs persisted. One day while sitting on the ward porch he had an

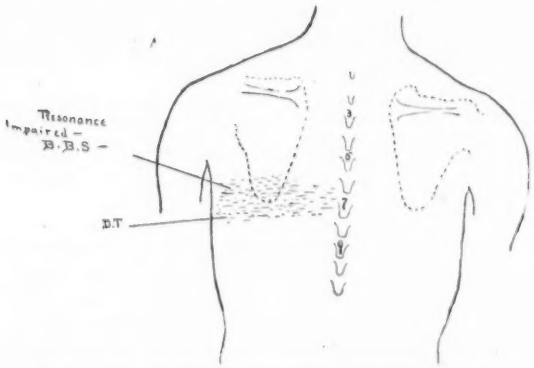


FIG. 4.—Atypical signs in empyema. Posterior view of same case as shown in Fig. 3: Shading, impaired resonance to flatness; *A*, hyperresonant; *B*, skodaic resonance to amphoric; *D.T.*, "dry tap," *i. e.*, fluid not found; *X*, fluid determined by puncture; *B.B.S.*, bronchial breath sounds; *R*, rales, crepitant and subcrepitant.

attack of severe coughing and began to bring up pus. Some was lost, but the nurse saved over a pint as evidence of the correctness of the diagnosis. The patient made a perfect recovery. I know of

no guide that is infallible; certainly physical signs are often enough misleading. In many cases, however, there can be detected, by

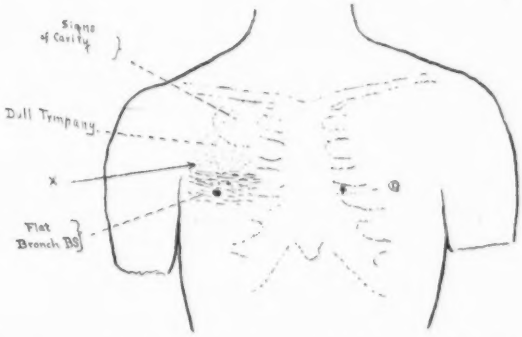


FIG. 5.—Atypical signs in empyema. Anterior view; Shading, impaired resonance to flatness; *A*, hyperresonant; *B*, skodaic resonance to amphoric; *D.T*, "dry tap," *i. e.*, fluid not found; *X*, fluid determined by puncture; *B.B.S*, bronchial breath sounds; *R*, rales, crepitant and subcrepitant.

careful examination, some spot where pressure produces acute pain, and I have found that this area of hyperesthesia is the most promising site for exploration. The accompanying illustrations

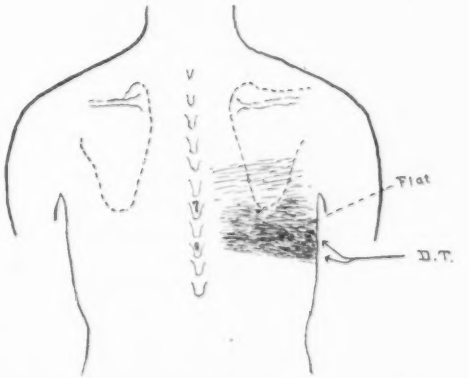


FIG. 6.—Atypical signs in empyema. Posterior view of same patient as shown in Fig. 5: Shading, impaired resonance to flatness; *A*, hyperresonant; *B*, skodaic resonance to amphoric; *D.T*, "dry tap," *i. e.*, fluid not found; *X*, fluid determined by puncture; *B.B.S*, bronchial breath sounds; *R*, rales, crepitant and subcrepitant.

(Figs. 3, 4, 5 and 6) are of some interest, not only in depicting the peculiarity of physical signs in some cases of empyema but also in

showing that several unsuccessful explorations do not prove the absence of fluid. There is no explanation for the fact that the area of maximum flatness is needled so often with no result, and a proximate hyperresonant area is shown by puncture to overlie fluid. It must also be borne in mind that there may be more than one separate collection of pus.

Finally, in the diagnosis of empyema I cannot too strongly disagree with the teaching that there is always a displacement of neighboring viscera, *i. e.*, heart or liver. Abscesses in the pleura of considerable size can develop in a lung bound down by adhesions without appreciable displacement of neighboring organs. On the other hand, marked emphysema in the uninvolved lung may produce displacement of the heart toward the diseased side. This fact has been noted at autopsy.

In the treatment of these cases of empyema the conception no longer holds that diagnosis should be followed by immediate thoracotomy. Early operation, before firm adhesions have been formed surrounding the suppuration, leads to pneumothorax and infection of the whole pleural cavity. The mortality under these circumstances is known to be high. Repeated aspirations, on the other hand, allow time for adhesions to form; the patient during this interval recovers to some extent from the severity of the infection, and, when finally subjected to operation, not only is the local condition in the lung walled off and better suited for drainage, but the patient's general resistance is higher and he is better able to withstand the shock of operation. A small percentage (in my experience about six) of the cases of empyema will recover following repeated aspiration alone and never require surgery.

The question arises at this juncture, For how long a period should aspirations be continued: in other words, for how long can operation be postponed? The answer is not as difficult as it might seem. So long as the patient continues to improve operation can be deferred. The criteria for improvement are better appetite and sleep, a lower fever and pulse-rate and evidences of diminished infection, such as less sweating and improvement in the patient's sense of well-being and strength. On the average this period of improvement will continue for about ten days. With a few the period is prolonged into convalescence. In some cases the reason for final operation is that the pus becomes so thick that drainage cannot be effected through a large needle. With others the indication for operation is an increase in the temperature, a failing appetite and the general appearance of the patient.

Of the relation of pulmonary abscess to bronchopneumonia we have but little knowledge. In three of my cases of abscess of the lung the history indicated very strongly a beginning of the affection in bronchial pneumonia. In one of these cases this is more than

probable, since the pneumonia developed after operation, the so-called ether pneumonia. The reason for mentioning pulmonary abscess in the present connection is that occasionally pulmonary abscess can be cured by artificial pneumothorax. This procedure is indicated, however, only when there are no pleural adhesions, since, of course, with such adhesions the desired collapse of the lung cannot be produced. In two cases, where the abscess was in the mesial portion of one of the lower lobes, artificial pneumothorax resulted in an abatement of the symptoms and the last case treated is well up to the present time, a period of about two years since treatment was discontinued. When the abscess is near the pleura, as unfortunately it frequently is, adhesions usually occur and the only cure under these circumstances is lobectomy.

The most common of the sequelæ of bronchopneumonia, alike with lobar pneumonia, relates to the heart. Slight involvement of the myocardium, as manifested by breathlessness on exertion, is so common, following all types of pneumonia, that it is to be regarded as one of the incidents of convalescence. With not a few individuals, however, this symptom is prolonged for a number of months. Affections such as described are by no means confined to the elderly or to those who have some preëxistent cardiac disorder, but are manifested not infrequently in robust young men. The physical signs are seldom clear cut, and of themselves would hardly disclose the nature of the disorder. The heart sounds may not be as clear as they should be and occasionally a systolic murmur can be heard at the apex. But these signs can be noted in a considerable number of apparently healthy persons. The significant fact is the symptoms of circulatory embarrassment coming on after an acute infection. From a therapeutic point of view it is important first to recognize the nature of the disorder, with a view to protecting the patient against premature severe physical exertion. Time alone corrects the great majority of these disabilities. In addition, well-supervised graduated exercises have a distinct use, as was demonstrated on such a large scale in the military convalescent camps.

In conclusion, it is desirable to emphasize that bronchopneumonia is a common affection in young, robust individuals, and that, on account of the physical signs, the disease may, in mild cases, be easily overlooked. The treacherous character of bronchopneumonia and the seriousness of its complications and sequelæ indicate the importance of early recognition and adequate protective care.

EXPERIMENTAL STUDIES IN DIABETES:

SERIES II. THE INTERNAL PANCREATIC FUNCTION IN RELATION TO BODY MASS AND METABOLISM.

II. CHANGES IN ASSIMILATION BY ALTERATIONS OF BODY MASS.

By Frederick M. Allen, M.D.,
NEW YORK.

(From the Hospital of the Rockefeller Institute for Medical Research, New York.)

The preceding paper[1] was a study of the alterations of assimilation produced by changing the mass of the pancreas. The present one deals with the alterations of assimilation produced by changing the body mass. Attention was first given to these relations in obese dogs.

I. PANCREAS AND BODY MASS RELATIONS IN OBESE DOGS.

The following conclusions were drawn (Table I):

1. No anatomic differences were found between different ages or different types of obesity. At one extreme are young animals which are fat apparently for the sole reason that they eat enormously and are very lazy. At the other extreme are a type well known to those who handle many dogs, namely, animals in advanced senility, toothless or with teeth worn to the gums, excessively obese and sluggish, generally either surly or stupid, and consuming sometimes a large and sometimes a surprisingly small quantity of food. Both types of animals in the above series were free from either gross or microscopic changes in the pancreas; in particular, from either fibrous or fatty invasion or island changes. If it is permissible to apply these observations to human pathology, it may be concluded that such changes in the pancreas are a distinct abnormality and not naturally attendant upon either obesity or senility.

2. Even with the extreme degrees of obesity here represented, the ratios of pancreas weight to body weight fell within the normal limits shown in Table II, Paper 1 of Series I.[2] This is not because this ratio does not change when an animal becomes fat, but merely because the variations in the ratio in different normal dogs are so wide. It is therefore not possible to demonstrate an abnormal susceptibility to diabetes in obesity on the basis of a reduced mass of pancreas in proportion to the body mass.

[1] Allen, F. M.: Am. Jour. Med. Sc., 1920, clx, 781.
[2] Allen, F. M.: Jour. Exp. Med., 1920, xxxi, 366.

3. It was mentioned in the preceding paper that alterations of body weight, apart from starvation or cachexia, do not change the glucose tolerance of normal dogs. Similar tests upon obese animals have shown no departure from the normal assimilation, as far as interpretation was possible. Protocols are omitted because there can be no claim to accuracy in comparisons, since reckoning dosage on the obese weight is obviously unfair and only guesses could be made of the normal weight. Nevertheless any serious reduction of tolerance would have been evident, and the conclusion is justified that neither obesity nor senility *per se* involves any demonstrable lowering of glucose assimilation.

TABLE I.—PANCREAS AND BODY MASS RELATIONS IN OBESE DOGS.

No.	Body weight, kgm.	Weight, total pancreas, gm.	Grams of pancreas per kgm. body weight.	Weight of remnant, gm.	Size of fraction.	Diabetes.	Remarks.
1	6.5	17.6	2.71	1.50	$\frac{1}{11}$–$\frac{1}{12}$	....	Senile, excessively obese; cachexia without glycosuria.
2	7.0	14.7	2.10				
3	7.2	12.2	1.69	1.30			
4	8.9	19.3	2.17	...	...	....	Age three years.
5	9.3	22.8	2.45	2.90	...	....	Senile.
6	9.7	22.0	2.27	...	...	....	Old.
7	12.0	26.3	2.19	3.40	$\frac{1}{4}$	Mild with removal of 0.85 gm. additional in 3 subsequent operations	Obese young dog.
8	14.3	30.8	2.15	3.25	...	....	Moderately old and fat.
9	14.8	31.3	2.11				
10	14.9	32.5	2.18	1.65	$\frac{1}{20}$	Gravis	Age four years.
11	16.4	35.2	2.42	5.60	$\frac{1}{6}$–$\frac{1}{7}$	....	Not excessively obese.
12	17.0	31.6	1.86	4.60	$\frac{1}{4}$	Levis	Age three years.
13	18.6	22.9	1.61	4.25	$\frac{1}{5}$–$\frac{1}{6}$	Levis	
14	18.6	39.2	2.11	...	...	....	Age six years.
15	19.0	36.3	1.86				
16	19.2	31.0	1.61				
17	19.5	36.3	1.81	1.20	$\frac{1}{30}$	Gravis	
18	20.0	28.4	1.42	5.50	$\frac{1}{5}$	....	Death in three days.
19	20.5	41.0	2.00	12.00	$\frac{1}{3}$–$\frac{1}{4}$	....	Age four years; normal wt. estimated at 13 kilos.
20	20.9	37.7	1.80	2.90	...	....	Old.
21	22.8	33.4	1.46	1.30	$\frac{1}{16}$	....	No glycosuria; death within three days.
22	22.8	41.1	1.80	7.50	$\frac{1}{2}$–$\frac{1}{3}$	None	Age six or seven years.
23	24.3	42.9	1.76	6.10	...	....	"Rather old."
24	25.0	51.2	2.04	6.50	$\frac{1}{3}$	Gravis	Fat but not pathologically obese; glycosuria in spite of prostration.
25	28.5	46.3	1.62	...	...	....	Moderately obese.
26	32.4	61.3	1.89	12.4	$\frac{1}{2}$	Transitory with prolonged glucose diet.	

4. The types of obese dogs mentioned react differently to partial pancreatectomy. The younger ones generally withstand the operation well. The senile ones very commonly die within one to three days, presumably of the pancreatic intoxication which is called "fat necrosis" from one of its minor accompaniments. The deaths are not due to ordinary shock, because such animals safely undergo control operations involving more trauma and exposure of viscera and sometimes survive total longer than partial pancreatectomy. Senility is not always a factor, because a few younger dogs with a type of obesity apparently due to endocrine disorder likewise die abruptly after such operations, while some of the old obese kind which retain greater liveliness survive. Injections of pancreas extract have not conferred immunity, but it is sometimes possible to immunize the animals by successive operations, removing only a very small piece of pancreas the first time. The results are not very satisfactory, because the dogs generally either lose their obesity or die before the series of operations is complete.

5. The main question under consideration was whether obese dogs would for any reason be more susceptible to diabetes than normal dogs. The results with dogs Nos. 12, 13, 24 and 26 in Table I suggest that this may be the case. Diabetes was not produced in any of these animals with larger pancreas remnants than in some of the normal dogs of Paper 1, Series I, but the proportion of positive to negative results with remnants of this size is much higher in the obese series. This latter series is, however, so short that no positive conclusion is warranted.

II. ALTERATIONS OF BODY WEIGHT IN THE SAME ANIMAL.

It was concluded in Series I that various influences can be most accurately judged by applying them to partially depancreatized animals and observing the individual alterations of assimilation. One important procedure would be to depancreatize a dog just short of diabetes and then determine whether the most extreme fattening could actually bring on diabetes, *i. e.*, whether obesity can ever be a genuine cause of diabetes to an extent equal to the removal of a small fraction of a gram of pancreatic tissue. This point was not covered by this investigation because of the practical difficulties. The method actually used consisted in taking diabetic dogs free from symptoms on fixed diets and studying the changes of assimilation produced by alterations of the nutritive level. Changes of tolerance in inverse relation to the body weight were mentioned incidentally in Series I, without strict proof of the causal character of the relation. The present experiments were

designed to furnish such proof, on different diets, but particularly including changes of weight produced entirely by changes of the non-sugar-forming element of the diet, namely, fat. The difficulties of carrying through such long experiments successfully were referred to in Series I.

Dog B2–10.

Female, mongrel, white, aged nine months, good condition; weight, 7 kilos.

November 18, 1913, removal of pancreatic tissue weighing 16 gm. Remnant about main duct estimated at 1.8 gm. ($\frac{1}{10}$). There was glycosuria as high as 4 per cent., which with onset of distemper diminished in spite of bread and glucose feeding and disappeared December 1. Weight was rapidly lost through anorexia and diarrhea. The lowest level reached was 4.4 kilos. With gradual recovery from the distemper weight was gained on plain bread and soup diet, and glycosuria ensued when the level of 5.1 kilos was attained on February 19. The diet was then changed to beef-lung *ad libitum*, glycosuria remained absent, and in subcutaneous tolerance tests in March and April there were traces of glycosuria with 2 gm. glucose per kilo (reckoned on the original 7 kilos weight), but none with 1.8 gm. or less. The weight, which was slowly increasing, was 6 to 6.3 kilos during this time. By July 29 the dog was obese at a weight of 10.4 kilos, and on this date glycosuria appeared and persisted during the following week until checked by fasting and reduced diet.

Dog C3–20.

Male, mongrel, brown, aged six to eight years; fair nutrition; weight, 24 kilos.

June 24, 1915, four-fifths of the pancreas was removed and additional tissue on July 16 and 30. Glycosuria was present on glucose and bread feeding, but ceased, and on plain bread diet on August 15 the plasma sugar rose only to 0.143 per cent. and was 0.088 per cent. the following morning. August 16 an additional 0.6 gm. of pancreatic tissue was removed and the diet was changed to beef-lung *ad libitum*. The weight at this time had fallen to 21.3 kgm. On August 25 the plasma sugar during digestion rose to 0.154 per cent., *i. e.*, higher on protein diet than on carbohydrate prior to the last operation. On September 29, at a body weight of 24.8 kilos, the plasma sugar was 0.077 per cent. immediately before feeding, 0.078 per cent. immediately after feeding and 0.161 per cent. five hours later. October 23, at a body weight of 25.8 kilos, glycosuria of 1.1 per cent. suddenly appeared and ceased

only with two days of fasting. The former diet was then resumed and on November 1 sugar suddenly reappeared in the urine in 2.4 per cent. concentration.

Dog B2–52.

Female, bull terrier mongrel, brindle, aged five or six years; excellent condition; weight, 12.8 kilos. April 24, 1914, seven-eighths of the pancreas was removed, and glycosuria proving transitory, half the remnant was removed on May 18. The weight meanwhile had fallen to 9.3 kgm. Glycosuria was immediately checked by fasting and a diet carefully built up, beginning with 50 gm. beef-lung and 50 gm. suet, and increasing so that by June 15 the dog was eating 1000 to 1200 gm. lung without glycosuria. July 30, glycosuria began with 0.53 per cent. sugar in 507 c.c. urine, followed by 1.6 per cent. in 836 c.c. the next day, at a body weight of 11.4 kgm. Continuous fasting to August 12 then reduced the weight to 9.3 kgm. as before, and the diet was built up as before. The dog would no longer eat the full quantity of lung, and it was necessary to introduce 50 to 100 gm. lard for fattening. On the lard and quantities of lung below 1000 gm., glycosuria remained absent until November 25. Then at a body weight of 12.5 kilos glycosuria of 0.4 to 2 per cent. was present for four days, ceased with a single fast-day, remained absent on the regular diet for a week, then on the same diet was present for two weeks, the weight during this time ranging as high as 14.3 kgm. and the animal appearing in splendid condition. It was then found impossible to stop the glycosuria, and after two weeks of fasting the dog died of acidosis.

Dog B2–57.

Female, mongrel, yellow, aged five years, good condition; weight, 11 kilos. Fasting from May 4 to May 21, 1914, reduced the weight to 8.7 kilos. On the latter date 19.6 gm. of pancreatic tissue was removed, leaving a remnant estimated at 2 gm. ($\frac{1}{11}$). Glycosuria remained absent while the diet was gradually built up.

June 14, at a body weight of 7.5 kgm., a diet of 1200 gm. beef-lung was begun, and the dog ate this quantity daily without glycosuria until July 30. On this date there was 0.38 per cent. glucose in 390 c.c. urine and the next day 1.7 per cent. in 635 c.c., the body weight being 10.4 kilos.

Fasting was then continued to August 12, reducing the weight to 8.1 kilos. The diet was then built up gradually to 500 gm. lung on August 22, the weight being 7.7 kgm. on that date. The dog

remained without glycosuria on this diet to September 14, when the weight had declined to 7.4 kilos.

September 14, 50 gm. lard was added to this diet, increased on October 5 to 100 gm. October 20, at a weight of 10.8 kgm., lard was stopped because the dog was tired of it, and the lung was increased to 1000 gm. daily. The dog was on this diet to November 13 and gained weight to 11.4 kilos.

November 13, 50 gm. lard was added, increased on November 18 to 100 gm. The lard was now eaten and considerable of the lung was left uneaten. December 24 the weight had risen to 16.3 kilos, which was marked obesity. Glycosuria then began and continued (0.3 to 4.2 per cent.) on the same diet to January 4.

Fasting then stopped the glycosuria in two days, but was continued five days, reducing the weight to 14.25 kilos. Lung feeding was then begun cautiously, with 100 gm. the first day to 500 gm. on January 14, when glycosuria of 0.18 per cent. appeared in 186 c.c. urine. This increased to 1.4 per cent. in 240 c.c. urine and ceased with a single fast day, but successive attempts at feeding now caused glycosuria more easily, until on January 31 it resulted from only 150 gm. lung. Fasting then proved unable to stop the glycosuria, and the dog died March 1, still showing 0.9 per cent. sugar in 1295 c.c. urine, with a body weight of 6.8 kilos.

Dog B2–79.

Male, bull terrier mongrel, brindle, aged four or five years, medium nutrition; weight, 15 kilos. November 10, 1914, removal of pancreatic tissue weighing 32.2 gm. Remnant about main duct estimated at 4.7 gm. ($\frac{1}{5}$).

Glycosuria following operation on bread diet ceased on a diet of 800 gm. beef-lung. From February 16 to April 2, 1915, the diet was 1000 gm. of lung, but the dog was cachectic and lost weight down to 11.2 kilos. The diet was then changed to bread and soup *ad libitum*, with benefit to the general health, and glycosuria remained absent to April 7, when the diet of 1 kilo of lung was resumed. The dog was anemic at this time, with a red cell count of 2,700,000, but began then to improve in digestion and health, gradually regained the original weight and vigor and was used for exercise and other incidental experiments, which did not lower the tolerance. The exercise in fact seemed to prevent glycosuria, as described in the following paper.

In September glycosuria could no longer be restrained on the diet of 1 kilo of lung but was absent on a diet of 500 gm. lung and 500 gm. suet. The dog was greedy for the suet, and by October

3 was obese at a weight of 17 kilos. Glycosuria of 0.77 to 1.5 per cent. was then present October 3 to 6.

October 7 to November 8 the dog was fed nothing but suet or lard. At first these were eaten abundantly, but at the end both appetite and digestion were spoiled. The weight diminished to 13.5 kilos. Glycosuria ceased the first day and blood sugar analyses reported elsewhere showed that the fat had no tendency to create hyperglycemia. Nevertheless, when a diet of 500 gm. lung was begun on November 9, glycosuria (0.84 per cent. in 323 c.c.) appeared on November 11, *i. e.*, there was not the rise of tolerance which occurs with such a fall of weight under other conditions.

Glycosuria was then kept absent with reduction of protein, while the weight was kept slightly below and above 14 kilos by the use of as much fat as the dog would take. Beginning December 7, the diet was 300 gm. lung and 200 gm. suet. Glycosuria was absent until January 2.

January 2, 1916, there was glycosuria of 1.5 per cent. in 194 c.c. urine, ceasing with a single fast day. Again, the protein was diminished, making the diet 200 gm. lung and 200 gm. suet. The weight was 14.2 kilos. It was possible to increase the suet to 300 gm. and then to 400 gm., so that by January 30 the dog weighed 14.9 kilos. Glycosuria then returned; no fasting was employed to check it, and the dog was allowed to pass on into hopeless diabetes.

Dog B2–80.

The earlier history of this animal was given in Paper 2 of Series I.[3] The carbohydrate diet and glycosuria in April and early May, 1915, were carried to such a point that the dog could not tolerate 1000 gm. of lung at a weight of 15.5 kilos. Repeated trials of this diet, interspersed with fast days, reduced the weight by June 2 to 13.2 kilos. The kilo of lung was then tolerated until June 9, when there was 0.17 per cent. sugar in 681 c.c. urine, followed by 0.72 per cent. in 607 c.c. the next day.

The glycosuria ceased with a single fast day and the diet was changed to 500 gm. lung and 300 gm. suet. Weight was gained very rapidly and on June 21 there was a return of glycosuria at a weight of 17 kilos.

This glycosuria required two days of fasting to stop and the protein was then further reduced, making the diet 250 gm. lung and 300 gm. suet. The weight continued to increase and the dog had the appearance of splendid health. The photograph at the end of Series I[4] was taken July 2, at a weight of 18.2 kilos. On July

[3] Allen, F. M.: Jour. Exp. Med., 1920, xxxi, p. 383.
[4] Ibid., Fig. 7, Plate 66, following page 608.

10 there was a sudden appearance of 1.4 per cent. sugar in 605 c.c. urine.

After two fast days to stop the glycosuria the diet of 250 gm. lung and 300 gm. suet was resumed and the dog was used for exercise experiments, as described in the following paper. Increasing glycosuria and acidosis led to death in coma on August 14.

Dog B2–01.

Female, large fox-terrier mongrel, aged two years, good condition; weight, 14 kilos. This dog was received October 25, 1913, and used first for successive removals of pancreatic tissue and tests of the tolerance as described in the preceding paper. Diabetes was finally produced by the removal of 0.8 gm. pancreatic tissue on August 31, 1916. The following record contains some details already referred to in the preceding paper and in Series I.[5]

Summary. Beginning September 1, 1916, at a weight of 11.4 kgm., the dog was free from glycosuria not only on unlimited bread diet but even with addition of 300 gm. glucose. With continuance of plain bread feeding and a slight gain of weight to 11.7 kgm. the tolerance by November 15 had fallen so that a considerable percentage of glycosuria resulted from giving 56 gm. glucose by stomach tube. The fall in tolerance was further indicated by the repeated glycosuria on bread diet up to December 25; sugar would appear and be checked by fasting; a few days later it would reappear and be checked again; and notwithstanding the slight loss of weight, there was the usual gradual decline of tolerance on this program, as indicated by the two days of fasting necessary, December 26 to 27, in contrast to the single days which previously sufficed.

From December 28, 1916, the only food given was a quantity of bread and soup mixture measured in a cup so as to be roughly uniform though not weighed, and representing a slight undernutrition diet, so that there was a gradual fall in weight to 9 kgm. on February 22, 1917. The tables show that at this low weight the blood sugar was normal both before feeding and during digestion of this diet, and the assimilation as judged by a test-meal on February 23 was notably higher than at the higher weight in the preceding November.

Beginning February 24, 100 gm. beef-lung and 100 gm. suet were given daily in addition to the above cup of bread and soup, so as to fatten the dog. The weight thus rose to 14.5 kgm. on June 8 and to 15.25 kgm. on June 12. Glycosuria occurred on June 8, was absent the next day and was continuous June 10 to 12.

[5] Allen, F. M.: Jour. Exper. Med., 1920, pp. 396, 564, 570, 600.

TABLE II.—DOG B2–01.

Date.	Weight, kgm.	Diet.	Remarks.
1916.			
Sept. 1–4	11.4	Bread and soup *ad libitum*	No glycosuria.
5	11.5	Same, with 100 gm. glucose	No glycosuria.
6	11.5	Same, with 200 gm. glucose	No glycosuria.
7	11.5	Same, with 300 gm. glucose	No glycosuria.
8–Nov. 14	11.5–11.7	Bread and soup *ad libitum*	No glycosuria.
Nov. 15	11.7	56 gm. Merck glucose in 30 per cent. solution by stomach tube (4 gm. per kgm. on 14 kgm. weight; no other food)	Before feeding, sugar neg.; two hours after, 18 c.c. urine, glucose 6.28 per cent.; five and one-half hours after, 38 c.c. urine, glucose 4.64 per cent.
16–30	11.6–11.1	Bread and soup *ad libitum*	No glycosuria except with tests (see below).
Dec. 1	11.1	Bread and soup *ad libitum*	1.5 per cent. sugar in 743 c.c. urine.
2	11.1	Bread and soup *ad libitum*	1.85 per cent. sugar in 581 c.c. urine.
3	.....	Fasting	No glycosuria.
4– 9	11.0	Bread and soup *ad libitum*	No glycosuria.
10	11.0	Bread and soup *ad libitum*	0.65 per cent. sugar in 1025 c.c. urine
11	11.0	250 gm. beef-lung	No glycosuria.
12–16	.....	Bread and soup and 100 gm. lung	No glycosuria.
17	.....	Bread and soup and 100 gm. lung	Slight glycosuria.
18–19	10.9	Bones only	No glycosuria.
20–24	.....	Bread and soup and 100 gm. lung	Slight glycosuria.
25	11.2	Bread and soup and 100 gm. lung	0.6 per cent. sugar in 260 c.c. urine.
26–27	.....	Fasting	Glycosuria ceased December 27.
Dec. 28, 1916–Feb. 22, 1917	Gradual fall to 9	Small cup of bread and soup daily	No glycosuria except with tests (see below); on February 19, plasma sugar before feeding 0.091 per cent. six hours after 0.133 per cent.
Feb. 24–June 7	Gradual rise to 14.5	Same cup of bread and soup, with 100 gm. lung and 150 gm. suet	No glycosuria except with tests (see below); on February 24, plasma sugar before feeding 0.102 per cent.
June 8	14.5	Same	0.9 per cent. sugar in 105 c.c. urine.
9	.....	Same	No glycosuria.
10	.....	Same	0.5 per cent. sugar in 160 c.c. urine.
11	.....	Same	Slight glycosuria.
12	15.25	Same	0.4 per cent. sugar in 200 c.c. urine.
13–July 2	Gradual rise to 16.6	400 gm. lung and 200 gm. suet; no bread	No glycosuria except with tests (see below); on June 30, plasma sugar before feeding 0.147 per cent.
July 3–Nov. 14	Gradual fall to 9.6	450 gm. lung only	No glycosuria except with tests (see below).
Nov. 15	9.6	450 gm. lung and 50 gm. bread	Faint glycosuria.
16	.....	450 gm. lung and 100 gm. bread	No glycosuria.
17	.....	450 gm. lung and 200 gm. bread	Slight glycosuria.
18–Dec. 20	Gradual fall to 8	450 gm. lung only	No glycosuria except with tests (see below); on December 2, plasma sugar before feeding 0.044 per cent., four hours after 0.110 per cent.
Dec. 21–30	Gradual rise to 8.75	Lung and suet *ad libitum*, with small cup of bread and soup	No glycosuria; on December 27, plasma sugar before feeding 0.145 per cent., four hours after 0.164 per cent., seven hours after 0.147 per cent.
Dec. 31, 1917–Feb. 13, 1918	Gradual rise to 9.2	400 gm. lung and 50 gm. suet	No glycosuria; on January 15, plasma sugar before feeding 0.110 per cent., six hours after 0.130 per cent.; on February 4, plasma sugar before feeding 0.089 per cent.
After Feb. 13, 1918	Gradual rise	400 gm. lung and 100 gm. suet	No glycosuria up to August, 1918.

Beginning June 13 the diet consisted of 400 gm. lung and 200 gm. suet without carbohydrate. The weight rose to a maximum of 16.6 kgm., and the standard test-meal on June 26 showed a marked fall in assimilation. There was no other glycosuria, but evidently continuous hyperglycemia, as judged by the plasma sugar of 0.147 per cent. before feeding June 30.

Beginning July 3 the diet was only 450 gm. lung, in order to give low calories with as much protein as in the former diets. The weight thus fell gradually to 8 kgm. on December 20. On November 15, the addition of 50 gm. bread caused transitory glycosuria, as frequently results from carbohydrate after a carbohydrate-free diet; but there was none with 100 gm. bread the next day and only a slight reaction with 200 gm. on November 17. Rising assimilation was also indicated by the feeding tests of October 5, November 22 and December 18 (Table III). The hypoglycemia present on December 2 (and presumably the following days) corresponded to the emaciation and cachexia.

Beginning December 21 the diets were such as to produce gain in weight. Up to December 31, bread in quantities similar to those given a year previously was tolerated without glycosuria but with hyperglycemia. Bread was then omitted and the weight steadily rose on protein and fat.

Events prevented further accurate tests, but glycosuria was absent up to August, 1918, and the animal was fat at that time. Paper 5 of Series I[6] gave the subsequent history up to death on October 15, 1919.

Remarks. 1. The first four tolerance tests (Table III) were arranged for judging the influence of the tests themselves. The quantity of 30 gm. glucose on November 20, 1916, was guessed at random, and proved smaller than desirable for a standard, as the glycosuria and hyperglycemia were too slight. A diet with 75 gm. glucose was given the next day and again on November 23. The test with 30 gm. glucose was repeated on November 27. As these closely spaced tests showed no significant differences between November 20 and 27 and November 21 and 23 it was concluded that the much less frequent subsequent tests could not be held responsible for any great changes of tolerance. This expectation was confirmed by the later observations of upward as well as downward fluctuations of the assimilation.

2. Attention may again be called to the close reproduction of typical human histories in the record of such an animal. Starting with an excellent physical condition and a very high tolerance it may be said that the occasional tolerance tests correspond to a

[6] Jour. Exper. Med., 1920, xxxi, 600.

few violations of diet, but that otherwise almost continuous freedom from glycosuria was maintained; yet the course was downward to death from diabetes three years later. Such a clinical record might well be adduced as evidence of inherent and inevitable downward progress, yet the dietary causes in this animal are perfectly plain; and if the previous conclusion that such dogs are free from inherently progressive tendencies be well founded, it is evident that the diet was the sole cause in this instance.

TABLE III.—FEEDING TESTS. DOG B2-01.

Date.	Weight, kgm.	Plasma sugar, per cent.	Urine.			Remarks.
			Vol., c.c.	Glucose, per cent.	Total glucose, gm.	
Nov. 20, 1916	11.6	....	....	....	0.13	Fed 200 gm. bread, 100 gm. lung and 30 gm. glucose.
Before feeding	....	0.088	626	Neg.	....	
2 hours after	....	0.133	25	Very faint	....	
4 hours after	....	0.143	26	0.31	....	
6 hours after	....	0.164	18	0.27	....	
Nov. 21, 1916	11.6	0.094	230	Neg.	0.42	Fed 200 gm. bread, 100 gm. lung and 75 gm. glucose.
2 hours after	....	0.224	18	Faint	....	
4 hours after	....	0.256	30	0.68	....	
6 hours after	....	0.159	26	0.83	....	
Nov. 23, 1916	11.6	0.103	110	Neg.	0.33	Same diet as Nov. 21.
2 hours after	....	0.147	22	0.46	....	
4 hours after	....	0.182	22	0.38	....	
6 hours after	....	0.200	32	0.48	....	
Nov. 27, 1916	11.6	0.093	20	Neg.	0.20	Same diet as Nov. 20.
2 hours after	....	0.130	78	Very faint	....	
4 hours after	....	0.135	48	0.42	....	
6 hours after	....	0.095	27	Faint	....	
Feb. 23, 1917	9.0	0.135	46	Neg.	0.22	Same diet as Nov. 21.
2 hours after	....	0.128	17	0.42	....	
4 hours after	....	0.154	15	0.43	....	
6 hours after	....	0.178	21	0.43	....	
May 17	13.5	0.078	75	Neg.	4.79	Same diet as Nov. 21.
2 hours after	....	0.212	16	2.14	....	
4 hours after	....	0.244	34	5.18	....	
6 hours after	....	0.250	45	6.42	....	
June 26	16.6	0.132	7	Neg.	10.35	Same diet as Nov. 21.
2 hours after	....	0.345	32	2.99	....	
4 hours after	....	0.416	92	4.33	....	
6 hours after	....	0.370	110	4.93	....	
Oct. 5	11.5	0.133	21	Faint	1.69	Same diet as Nov. 21.
2 hours after	....	0.263	12	4.32	....	
4 hours after	....	0.250	15	4.23	....	
6 hours after	....	0.220	17	3.20	....	
Nov. 22	9.8	0.123	64	Neg.	4.85	Same diet as Nov. 21.
2 hours after	....	0.303	44	4.20	....	
4 hours after	....	0.256	27	5.61	....	
6 hours after	....	0.227	30	4.94	....	
Dec. 18	8.0	0.147	9	Neg.	0.21	Same diet as Nov. 21.
2 hours after	....	0.141	7	Faint	....	
4 hours after	....	0.175	11	0.78	....	
6 hours after	....	0.161	7	1.66	....	

3. This experiment was planned to include the question of the specific relation of carbohydrate to the pancreatic function, which was also raised in the experiment on Dog 428 in Paper 4 of Series I.[7] The initial high carbohydrate diets undoubtedly reduced the assimilation more rapidly and powerfully than any other food, and at all stages carbohydrate obviously created the greatest tendency to glycosuria. On the other hand this experiment demonstrated (still more strongly than that on Dog 428), in the period December 28, 1916, to February 22, 1917, that with undernutrition a diabetic animal may live on chiefly carbohydrate diet without glycosuria and with normal blood sugar. In addition to refuting any exaggerated ideas concerning carbohydrate as a sole and specific poison in diabetes, this serves to check too great simplicity in the interpretation of the action of dietary restriction. To some extent it is doubtless true that the food carbohydrate and the body glycogen give rise to glycosuria, and it might be assumed that fasting and restricted diet merely reduce these two sources of urinary glucose. But it is a safe assumption that an animal undergoing slight gradual undernutrition on a bread diet has more glycogen than on a diet of 400 gm. beef-lung and 200 gm. suet (especially in view of the known influence of fat feeding in diminishing glycogen). The experiment then shows that the blood sugar may be lower and the tolerance higher under the former than under the latter conditions. In other words, diabetic glycosuria must be governed by something deeper than merely the quantity of carbohydrate available either in the food or in glycogen.

4. Attention was also paid to the protein ration, which was kept nearly enough equal so that fluctuations in the tolerance could not be attributed to it. Presumably the sugar which caused the hyperglycemia of June 30, 1917, and also that excreted in the active diabetes of 1919, was derived from protein, but the assimilation of this protein obviously varied widely with changes in body weight.

5. The changes in body weight were due essentially to fat feeding and fat deposit, and an influence of fat in connection with sugar metabolism and diabetes is thus demonstrated. The question whether the relation to the internal pancreatic function is direct or indirect is not answered by this experiment. On one hand is the predominant effect of carbohydrate in breaking down assimilation, as already mentioned; in the initial mild stage it is doubtful if the tolerance could ever have been broken down by fat or any non-carbohydrate diet. On the other hand, even in the later stage, carbohydrate was apparently assimilated well and harmlessly at a low level of nutrition, while overnutrition gradually brought

[7] Jour. Exper. Med., 1920, xxxi, 581–586.

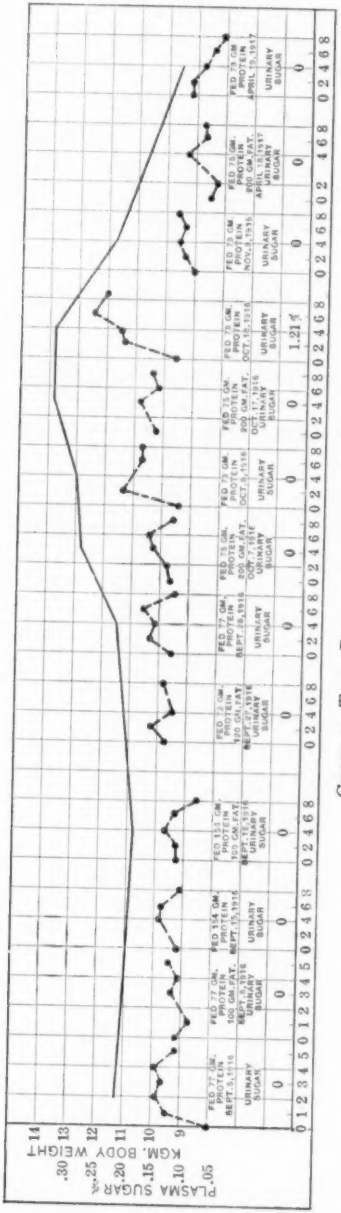

PLASMA SUGAR %
.30
.25
.20
.15
.10
.05
KGM. BODY WEIGHT
14
13
12
11
10
9
0 1 2 3 4 5 0 2 4 6 8 0 2 4 6 8
FED 77 GM. PROTEIN SEPT. 13, 1915
FED 77 GM. PROTEIN 200 GM. FAT. SEPT. 8, 1915
FED 154 GM. PROTEIN SEPT. 15, 1915
FED 154 GM. PROTEIN 200 GM. FAT. SEPT. 22, 1915
FED 77 GM. PROTEIN SEPT. 29, 1915
FED 77 GM. PROTEIN 200 GM. FAT. OCT. 7, 1915
FED 77 GM. PROTEIN OCT. 13, 1915
FED 75 GM. PROTEIN 200 GM. FAT. OCT. 17, 1915
FED 75 GM. PROTEIN OCT. 18, 1915
FED 75 GM. PROTEIN NOV. 1, 1915
FED 75 GM. PROTEIN 200 GM. FAT. APRIL 13, 1917
FED 75 GM. PROTEIN APRIL 19, 1917
URINARY SUGAR
0
1.21%

CHART OF TESTS PERFORMED ON DOG C3-86

on diabetes even in absence of preformed carbohydrate. In either case the overload of assimilation was manifested by glycosuria or hyperglycemia. There was no evidence of harm from either carbohydrate or gain of weight so long as these signs of overstrain of the carbohydrate side of metabolism were avoided; but forcing either the carbohydrate ration or the total nutrition beyond the limits set by these danger signals resulted in downward progress and finally hopeless diabetes.

Dog C3-86.

Female, mongrel, brown, aged two or three years, slightly obese; weight 15 kilos. April 28, 1916, removal of pancreatic tissue weighing 33 gm. Remnant about main duct estimated at 2.9 gm. ($\frac{1}{12}$ to $\frac{1}{13}$). Glycosuria was checked by fasting and undernutrition and the dog was kept in this border-line condition under careful tests until it was established that the assimilation limit amounted to about 800 gm. of beef-lung and that this tolerance showed no further tendency to change spontaneously. Beginning September 5 a series of tests were performed, most of which were previously published,[8] and the two concluding ones are now added in the accompanying graphic chart.

The points of chief importance in this experiment are the following: (1) The protein of the diet was kept constant throughout and the changes of weight were produced solely by adding and withdrawing fat; (2) there was no indication of the conversion of fat into sugar—on the contrary, the plasma sugar curves were generally distinctly lower on the test days with protein plus fat than on the days with protein alone, probably because of slower absorption with the fat admixture; (3) under these conditions it was proved decisively that the assimilative power fell as the weight rose, and was restored even higher than the original level when the body weight was reduced below the original level.

III. ALTERATIONS IN BODY MASS IN THE FORM OF ACTIVE PROTOPLASM.

In the preceding paper has been described the phenomena resulting from reduction of the mass of the pancreas and in the present paper have been discussed the changes in metabolism resulting from the reduction of body mass in the form of reserves, especially fat, by alteration in diet. It now remains to discuss the changes resulting when the body mass is suddenly reduced through loss of body tissue, such as may occur following extensive

[8] Allen, F. M.: Am. Jour. Med. Sc., 1917, p. 153, Chart VIII.

injury, or following amputation. The latter is unfortunately frequently necessary in diabetic patients. Diabetic gangrene is still only too prevalent and if the infection is extensive thigh amputations are the rule. Occasionally both legs are thus lost. More often, with advanced arteriosclerosis and doubtful prognosis, the question must be decided whether to amputate at once or spend months in a risky attempt to save the limb. If a marked gain of assimilative power could be expected from the removal of one or both legs there are cases in which this would determine the choice. On the other hand, if there is danger of any lowering of assimilation from the removal of large masses of muscle this also should be known.

Theoretically it would seem possible that there is a quantitative relationship between the pancreas and the mass of body tissue which it must supply with hormone. As previously remarked, it must be impossible for the pancreas of a mouse to supply the body of an elephant. It is conceivable that the effects of over- and undernutrition may be due to changes in the mass as well as the activity of living protoplasm, according to one well-known theory. This involves also the question whether the pancreatic function pertains to the endogenous or the exogenous metabolism in the sense of Folin. Determinations of the urinary creatinin and uric acid in human patients would have been simple and instructive, but were prevented by circumstances; and those actually begun in dogs failed by reason of the difficulties already mentioned (in that the dogs chosen for the purpose prove unsuitable or meet with accidents), and repetition was not possible. It is evident, however, that sudden loss of a considerable bulk of cells carries away everything pertaining to these cells in both mass and metabolism, and the effects can be compared with those of a similar reduction of weight resulting from diet. There is some possibility that the effect may be much greater. Another possibility is that the loss of important masses of sugar-burning tissue, especially muscles, may lower the total capacity for sugar utilization.

Opportunities have occurred for the observation of dogs (both normal ones and those rendered diabetic by removal of portions of the pancreas), that have lost large amounts of body tissue suddenly. In one instance the loss was over 20 per cent. of the body weight. Tests made on these dogs by means of intravenous injection of sugar showed no definitely increased tolerance for carbohydrates in any of them.

The opinion that the endocrine pancreatic function is concerned in exogenous rather than endogenous metabolism is in line with certain theoretical deductions. If it has been possible to perform the desired analyses in clinical cases there is reason to anticipate that obese patients whose body protein is protected by diet and who are merely reduced in fat will not show any reduced output

of endogenous creatinin and uric acid. Yet diabetics of this type gain greatly in assimilative power under this program. Such a research would establish that the internal pancreatic function is not connected with the endogenous metabolism, so far as the latter is chemically measurable.

A practical point not covered by the animal observations is the assimilation per kilogram of the reduced body mass and the lower food requirement of a patient who has lost one or both legs. An indirect benefit to the diabetes from this fact can scarcely be doubted, but the point has no theoretical significance in the present connection, and as a practical measure it is scarcely to be mentioned in comparison with the therapeutic method of reducing the metabolism by undernutrition.

Conclusions. 1. The assimilative power of diabetic animals rises and falls inversely with the body weight. This change is established on different diets, which exclude the supposition that it is due merely to variations in either glycogen or protein, and which prove that it is produced also by the feeding and deposit of a non-sugar-forming material, namely fat.

2. When considerable masses of active tissue, especially muscle, are removed by amputation, the effects upon the assimilation are negligible compared with those of similar losses of weight produced by undernutrition. It may therefore be concluded that the effects of undernutrition are not due to a reduction of active protoplasm but rather to a reduction of food supplies and metabolism. Though there must necessarily be some relation between the mass of pancreas and the mass of body cells which it can supply with hormone, this research indicates a direct quantitative participation of this hormone in the metabolism of matter, and furthermore in exogenous rather than endogenous metabolism. In other words, the pancreatic function is not appreciably spared when the same quantity of food is metabolized by a reduced number of cells, but rather when the same number of cells metabolize a reduced quantity of food materials.

3. This principle is important clinically in that undernutrition should be continued to the point of relieving the pancreatic function from overstrain revealed by the most delicate tests, particularly hyperglycemia. With extremely few exceptions in human patients the curve of rising tolerance intersects the curve of falling weight at some level on which life can be maintained. Lack of thoroughness in relieving the pancreatic function is the chief cause of continued deterioration of this function and the consequent choice between coma and starvation. The present investigation has aimed at something more than an empiric treatment, namely, the valid proof of a quantitative relation between the internal pancreatic function and the total body weight and metabolism. Any theories of the nature of this function or of diabetes must

take account of the fact that the islands of Langerhans are concerned not merely in the combustion of sugar or storage of glycogen, but also in the maintenance of the general tissues and reserves. In some manner an increased supply of fat or formation of adipose tissue imposes a burden on the island function, and reduction of any kind of food or of the body weight reduces the demand upon this function. This fact seems to indicate that the island hormone has both a catabolic and an anabolic role.[10]

As the diabetic deficiency is so much more prominent with regard to carbohydrate, it is possible that the function is directly related to this alone, and that other foods are concerned only indirectly through their influence upon carbohydrate metabolism, though this point remains unproved. Whether the relation be direct or indirect, the status of the pancreatic hormone in general metabolism and of the disturbance of general metabolism in diabetes is sufficiently important that treatment must be directed to it and is seldom successful if limited to restriction of carbohydrate alone.

BENZYL BENZOATE IN PEDIATRIC PRACTICE.

By John Ruhräh, M.D.,
BALTIMORE, MARYLAND.

The writer became interested in this subject several years ago when Dr. David I. Macht was first working with this interesting and useful preparation.

Macht showed that the action of the opium alkaloids on smooth muscle fiber bears a direct relation to the chemical structure of the drug. The morphin group tend to stimulate contraction and to increase the tonus of smooth muscle while the papaverin group tend to inhibit contraction and to relax the tonus. He showed, further, that the stimulating action, on the one hand, is due to the pyridin part of the molecules and the relaxing properties to the presence of the benzylic grouping in their molecules. A search was made for a substance with a benzyl radical which would have the same action on smooth muscle but be free from toxic and narcotic principles. Macht finally settled on benzyl benzoate, a well-known organic ester, in commercial use in the manufacture of perfumes.

Benzyl benzoate, Macht also determined, was largely excreted in the urine as hippuric acid.

On the smooth muscle, benzyl benzoate inhibits the rhythmic contractions, lowers the muscle tone and relaxes spasm. The action

[10] Taylor, A. E.: Tr. Coll. Phys., Philadelphia, 1916, xxxviii, 254. Cf. Rockefeller Institute Monograph, 1919, No. 11, p. 128.

on the intestinal movements is similar to atropin, an inhibition of peristaltic action. On the uterus, gall-bladder and the urinary bladder the action is antispasmodic, inhibiting the contractions and causing relaxation. On the circulation the action is chiefly on the peripheral vessels, a fall in pressure due to the relaxing of the arterial muscles. As ordinarily administered the effect on the circulation may be disregarded, although it is given by mouth for its action on arterial hypertension. Ordinary doses do not affect the heart or respiration except as they may produce a quieting effect on the respiratory centers in certain pathologic states. Such doses do not affect the central nervous system and only very large doses affect the general musculature.

Therapeutically, Macht found the uses of the drug to be very much those which would be anticipated, *i. e.*, the inhibition of peristalsis and the relaxation of the spasm of smooth muscle.

In infants and young children many distressing symptoms are caused by the great tendency to spasm of the smooth muscles, and a brief consideration of the uses of benzyl benzoate in pediatric practice may be of service in stimulating further study of this drug, which, it would seem, bids fair to become a permanent part of our armamentarium.

On general convulsive conditions its action is often most favorable. This, perhaps, would scarcely be expected, but the clinical results have been very striking in infants who were having repeated convulsive seizures. There are certain children, and there are certain conditions, which doubtless cause a similar condition in any child, in which general convulsions are brought on by reflex action from what appears to be very slight causes, the so-called spasmophilic diathesis in the instance first named. One or two illustrative cases will suffice.

1. An infant, four days old when first seen. Delivery had been normal but a circumcision had been performed immediately after birth. This wound had become infected, and what appeared to be a general septic condition resulted. At some time each day the temperature reached 104° or 105° F. Omitting other irrelevant details it may be stated that the child was having forty to fifty convulsive seizures a day. The slightest movement about it was sufficient to provoke an attack. During the physical examination the child was in a constant state of spasm. Lumbar puncture was tried but no fluid could be obtained. Four-drop doses of benzyl benzoate, sufficiently diluted, were given and later the dose was diminished to one or two drops at four-hour intervals. The effect was all that could be desired. The number of convulsive seizures was diminished to about half dozen a day, the child was able to nurse with comfort and it eventually made an uneventful recovery.

2. A child of three, of extremely nervous parents and very nervous

itself, with the history of frequent convulsions, ate a variety of indigestible articles of food and started in with convulsions at frequent intervals. The stomach and bowels were emptied, but the convulsions persisted. Benzyl benzoate was administered in ten-drop doses and a condition of quietude resulted.

The first trials by the author were in whooping-cough. This disease presents certain peculiarities, among which is the notoriously uncertain action of antispasmodic drugs. What quiets one child will have but little effect in another. Taken all in all, belladonna or atropin gives the best results in the greatest number of cases, but atropin is a drug which cannot be left indiscriminately in the hands of the ever-increasing careless, and the same is true of most of the other powerful antispasmodic drugs. Benzyl benzoate acts fairly well in many cases, lessening the number of attacks of coughing and so making the patient more comfortable. The action is, however, uncertain. In some instances the relief is striking while in others it is practically *nil*. This may be due to lack of knowledge in the dosage, and it may be that in the resistant cases larger amounts would produce the desired effect.

In cases of bronchial asthma and in spasmodic bronchitis the effect is most happy, and in the author's experience most certain of all the diseases in which he has used the drug. The wheezing case of bronchitis is almost always converted into one with easy, silent respiration while the asthmatic is rendered tolerably comfortable, and this without the undesirable concomitant effects of most of the drugs ordinarily employed.

In colic due to spasm of the gastric or intestinal muscles relief is usually prompt, and in hiccough, sometimes a very uncomfortable symptom in early life, the results are more satisfactory than with any other drug with which the author is acquainted. Of course, the transient hiccough so commonly seen in young infants rarely needs treatment. In only the more severe and prolonged attacks is anything needed.

Of more importance and worthy of thorough investigation is the use of benzyl benzoate in pylorospasm. Of course, one should differentiate the cases in which the spasm predominates from those in which the obstruction is chiefly due to hypertrophy. Many cases supposed to be the latter may be permanently relieved by the use of antispasmodics, and the author has a long list of such cases in which atropin or papaverin has been successfully used. In fact, atropin has proved so satisfactory that the trial of any substitute made but little appeal. There are, however, cases in which the amounts of atropin required to cause relaxation will produce slight toxic symptoms, such as dryness of the mouth and throat and dilatation of the pupils. In such cases benzyl benzoate is of service and it has been successfully used in others. While apparently non-

toxic the taste and burning sensation make it more difficult of administration. For those unfamiliar with the correct dosage of atropin it is perhaps safer; but the fact remains that atropin poisoning rarely, if ever, kills and is not liable to occur except when simple directions cannot be followed.

In diarrhea in which there is excessive peristalsis, benzyl benzoate may be used to check the excessive movements, and it does not check secretion and it may eventually replace opium in cases in which there is a doubt as to the propriety of using opium.

In spastic constipation it is also of value. Curious cases of this are not infrequently met with in children, and may even find their way to the operating table. Atropin has been the chief reliance, but benzyl benzoate is of positive value. One instance may be cited:

3. A previously healthy fifteen months' old boy was taken suddenly in the early morning with severe pains in the abdomen, vomiting and a certain amount of prostration. Castor oil was immediately administered by the mother and an enema given resulted in a small stool. The castor oil was without effect. Following the enema there were no more bowel movements and a repetition later in the day brought away only a little mucus. The vomiting continued. He was first seen about thirty-six hours after the onset and after various drugs had been given without relief and the question of operation for obstruction had arisen. Ten drops of benzyl benzoate properly diluted were retained and in about an hour there was a copious evacuation, with immediate relief of pain and vomiting.

Several similar cases have been seen by the author in which atropin hypodermically in full doses gave relief; in one, a child of two, who was supposed to have an obstruction of the intestine. The child had eaten heartily of some dry, branny breakfast food. Some time later in the day there was vomiting and a bowel movement, great pain referred to the abdomen and prostration. Repeated enemas and purgatives gave no relief. When seen, thirty hours later, the child was greatly prostrated and a mass could be felt in the lower part of the epigastric region, somewhat to the right. A rectal examination brought away a small amount of fecal matter mixed with some particles of the food. A large dose of atropin gave relief and a large quantity of breakfast food was passed. It had evidently passed rapidly through the stomach and swelling in the intestine through the absorption of fluid and caused a spasm of the intestinal muscles above and below. The antispasmodic action of the atropin relaxed this, just as benzyl benzoate had caused relaxation in the case reported.

It hardly seems necessary to quote case histories illustrative of each phase of the usefulness of this drug. It would seem that in a

remarkably short time its place has been definitely made and one can safely predict it will continue in use until replaced by something better, or, at least, newer. Its limitations are scarcely known as yet but may easily be surmised. The dosage offers the greatest difficulty.

The author's experience has been limited to the use of a stable preparation prepared by Mr. H. A. B. Dunning, of Hynson, Westcott & Dunning, of Baltimore. Adults may take a dram of this at intervals of four to six hours as in dysmenorrhea. Macht gives the adult dose as 20 minims, but this will be found to be too small in many instances. For children the dose may be scaled down. Assuming the adult dose to be suited to 150 pounds, use either the amount obtained by the fraction of the child's weight and 150 or use Young's rule of the age divided by the age plus 12. Apply either of these to 60 minims as the maximum dose (not necessarily) to 40 minims as an average dose and 20 minims as a minimum dose.

The drug is hot and unpleasant to most children and must be diluted with water, sweetened water or milk. Older children may take it dissolved in olive oil and put up in capsules, but plenty of water should be taken at the same time. Carminatives are recommended to make the dose more palatable, but their use is of questionable value. Ampoules of benzyl benzoate in olive oil may also be had for hypodermic use when very rapid action is desired. When given by this method the drug should be injected intramuscularly.

The drug seems non-toxic. The author observed an instance when a dram was given by mistake to a child of six years. Apart from a disagreeable burning sensation in the mouth, throat and epigastrium no ill effects were noted. Whether the effects of the drug wear off with continued use, *i. e.*, a tolerance established, has not been determined.

Conclusions. Benzyl benzoate is a valuable addition to the armamentarium of the pediatrist. It may be used in place of atropin wherever a relaxing effect is desired on spasm of smooth muscle.

The author has used it sufficiently to be able to recommend it in bronchial asthma, spasmodic bronchitis, gastric or intestinal colic, hiccough and spasmodic constipation.

It has been recommended by others in excessive peristalsis.

In whooping-cough its action is often most beneficial, but the results are uncertain, as is the case with all other antispasmodics in this disease.

In general convulsive conditions not dependent on organic lesions of the central nervous system, especially in the newborn, the drug will be found of benefit.

It is non-toxic but not particularly agreeable to take.

STUDIES IN THE PHYSIOLOGY OF THE LIVER: I. TECHNIC AND GENERAL EFFECTS OF REMOVAL.

By F. C. Mann, M.D.,

ASSOCIATE PROFESSOR OF EXPERIMENTAL SURGERY AND PATHOLOGY, THE MAYO FOUNDATION, ROCHESTER, MINN.

The relatively large size of the liver, its double blood supply, and its elaboration of an internal and an external secretion have contributed to make the organ a source of continual interest to the physiologist. Many problems concerning its function are not definitely understood or are still under debate. They have been investigated by the removal of the liver and a study of the effect on the organism. The usual method has been to modify the function of the organ by performing an Eck fistula and ligating the hepatic artery, leaving the organ in place, the animal being kept under an anesthetic throughout the period of observation. This method may be satisfactory for the investigation of some problems, but the autolysis and absorption of the remaining liver tissue is a serious complicating factor. For instance, cutting off the blood supply to one lobe of the liver of a dog by ligation usually makes the animal very sick within a short time and causes its death in less than twenty-four hours. Various lobes of the liver have been removed by repeated operations, but the remaining portion always regenerated so that a permanent deficiency of liver tissue was not produced. In one of my experiments the surgical removal of approximately 70 per cent. of the liver was followed by practically complete regeneration in the course of a few months. The same condition follows the functional removal of the liver tissue by ligating the ducts. I have been able to ligate the ducts that drain approximately 70 per cent. of the liver without producing any effect on the animal's general condition. The ligated portion of the organ has undergone biliary cirrhosis and the unligated portion regenerated to make up for the loss of functionating liver tissue. The complete removal of the organ has been complicated by its relation to the portal circulation and the vena cava.

The portal circulation can be taken care of easily by an Eck fistula, but the intimate relation of the liver to the vena cava in most species of animals is such that complete removal of the organ rarely can be accomplished without damage to the venous return from the extremities. If damage to the vena cava is avoided, liver tissue is always left. Usually the remaining tissue is without blood supply and undergoes autolysis, producing a definite toxic effect.

For the study of some problems in the laboratory it seemed desirable to know definitely the course of events following the removal of the liver under conditions complicated by no factors other than the

anesthetic used at operation. None of the methods previously described fitted our purpose. Accordingly the method herewith reported for the removal of the liver of the dog was developed. The success of the method depends on the fact that the portal capillaries offer more resistance than collateral venous channels and as a result collateral circulation develops through other venous channels.

Technic of Removal of the Liver. The operation is performed in three stages. Ether anesthesia and sterile technic are employed. In the first operation an anastomosis is made between the portal vein and vena cava in the manner followed in performing an Eck

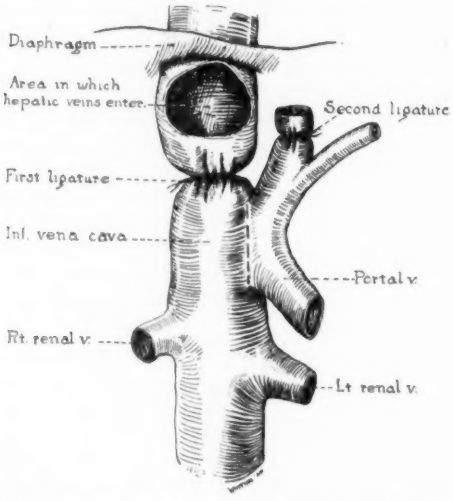


Diagram illustrating the steps in the technic of the removal of the liver. At the first operation the portal vein and vena cava are anastomosed along the dotted line and the first ligature is placed. At the second operation after the collateral circulation has been established the second ligature is placed. At the third operation the liver and the portion of the vena cava between the ligature and diaphragm are removed.

fistula, except that the vena cava is ligated instead of the portal vein. The ligature is applied just proximal to the entrance of the right lumbo-adrenal vein. This produces an increased pressure in both the vena cava below the ligature and in the portal system. Since the liver capillaries offer more resistance than that necessary to develop a collateral circulation through the azygos and internal mammary veins, in a short time most of the blood from the extremities will be passing through the latter route. The collateral circulation develops to such an extent that in three or four weeks after the first operation the second can be performed. The portal vein is ligated at the usual site in performing an Eck fistula, after which

all the blood from the posterior extremities and the portal system passes to the heart through the peripheral collateral circulation, see illustration. At the third operation the liver is removed completely by ligating the hepatic artery, the vena cava just below the diaphragm, and whatever small collateral veins have developed along the gastrohepatic omentum.

As in all experiments in which more than one operation is necessary, every experiment was not successful. In animals in which the diameter of the portal vein is narrow it is not always possible to ligate the cava without producing too much pressure in the portal system. Sometimes thrombosis occurs. In some animals the collateral circulation does not develop sufficiently to permit ligation of the portal vein. In a few cases a collateral circulation through thin-walled veins developed around the field of operation and resulted in unavoidable hemorrhage at the final operation.

The development of the collateral circulation has been interesting. In some animals, especially females, the superficial abdominal veins have returned most of the blood, anastomosing through the internal mammary veins. A very marked caput medusæ developed in these cases. In other animals there was little dilatation of the peripheral veins, the collateral circulation developing through the deep vessels. In some animals a considerable collateral circulation developed through the capsular veins of the kidney. In one animal the vena cava thrombosed throughout its entire length from the ligature to below its bifurcation. The animal lived for several weeks with the blood from the kidneys returning through the capsular veins. In some animals the esophageal anastomosis was markedly developed.

The length of time between the different operations varied. In most instances it was at least a month and longer between the second and third operations.

Most of the animals remained in good condition throughout the entire period of observation and afforded us an opportunity to obtain some data with regard to the Eck fistula and the reverse Eck fistula. Few facts of value can be obtained concerning the reverse Eck fistula unless the collateral venous return has been occluded. Since the blood flow through the liver was but temporarily increased this probably explains why little of note had previously been observed in a study of the latter.

Every effort was made to perform the final operation as quickly as possible and to use a minimum of the anesthetic. The removal of the liver from the beginning of the anesthetic seldom required more than one hour, and the animal recovered almost completely from the anesthetic within another hour. Artificial heat was usually supplied until the animal fully recovered. This was not found to be essential, however. The widely dilated veins usually occasioned some hemorrhage, but only infrequently sufficient to constitute a

serious complication. Such data as a pulse-rate, respiration, and temperature were taken before and at various intervals after operation.

An excellent illustration of the mechanical function of the liver in offering resistance to the diaphragm was obtained in the first experiment in which the third stage was attempted. After the liver was removed the animal's respiration remained very shallow. Artificial respiration by manual means was instituted to assist recovery. To our surprise the animal died immediately after the artificial respiration was started. Necropsy showed that the thoracic compression had ballooned out the diaphragm at the former site of the liver, and, owing to the lack of resistance previously offered by the liver, a simple exchange of pressure between the thoracic and abdominal cavities resulted without any exchange of air in the lungs. In the subsequent operations insufflation was employed and no further trouble was encountered.

Results of Removal of the Liver. In general the course of events following removal of the liver has been quite constant in the different animals. It was anticipated that by carefully following the technic described it would be possible to keep a dog alive for a considerable length of time. This hope was not realized as all the animals in this series died within five to eleven hours after operation. But even though the length of life after operation was short we were able to observe the course of events subsequent to total loss of liver function and under conditions closely approximating normal.

The period of recovery of an animal from the anesthetic and from the immediate effects of the removal of the liver does not seem to differ from the period of recovery following other operations; in our series it varied from one hour to two hours. After the animal recovers from the anesthetic there is an interval which in this series of experiments varied from two to eight hours, during which the animal appears to be normal. It then becomes moribund and usually dies quickly, within one or two hours.

Before the animal develops the symptoms apparently of loss of liver function, its condition as to pulse, respiration or temperature is identical with that of an animal at a corresponding time following any other operation which has involved a similar period of time, amount of trauma, and anesthesia. During the period following the recovery from anesthesia the animal walks around, responds to call, drinks water and sometimes milk. To all appearances it is normal, except, of course, for the signs of a recent operation.

The onset of the moribund period is usually sudden and the first sign is muscular weakness. The animal prefers to lie down, and when standing it cannot hold itself erect or avoid swaying when walking. Usually within an hour after the first evidence of muscular weakness the animal is unable to rise, but lies quietly breathing, with muscles flaccid and relaxed.

The period during which the animal is quiet is usually short. It is soon noted that a loud noise or a jarring of the table upon which it lies produces a stiffening of the limbs. Muscular twitchings develop and later definite convulsions occur. The twitchings may involve only one muscle in a limb or a whole group of muscles. They are both tonic and clonic in character. Usually shortly after the muscular twitching has developed a very slight noise or a sharp slap produces a general convulsion. Some of the muscular spasms last one-half minute or more.

Often the animal exhibits movements similar to those employed when trotting; just before death it attempts to vomit and the slightest stimulation around the region of the head produces a snapping of the jaws as though at an imaginary foe. Death follows a convulsion, involving seemingly all the muscles of the body.

After the removal of the liver the pulse is more rapid than normal, but not more so than is usual, following other comparable operative procedures. After muscular weakness develops the pulse decreases but does not go below normal.

The respiration always becomes rapid and frequently of the Cheyne-Stokes type as the animal develops the moribund condition. Death is respiratory rather than cardiac; respiration in our animals has always stopped before the heart.

Contrary to expectations the temperature continues normal until the animal becomes comatose, when it may become subnormal. An interesting observation is that in some of the animals the temperature may go a degree above what it was previous to operation just before muscular weakness develops.

No findings at necropsy have as yet been noted which could be attributed to the loss of the liver.

In many respects the syndrome following the loss of liver function is typical of the syndrome following the total removal of the adrenal glands; the initial development of a muscular weakness is quite similar. On the other hand the muscular twitchings, and, particularly, the muscular spasms and the character of the respiration recall parathyroid tetany. The condition following removal of the liver, however, is, on the whole, a definite entity.

Since the preparation of an animal for the final operation of removal of the liver takes considerable time and there are some failures at the various stages, so far only a small series has been studied. This series, however, has shown conclusively that a definite and constant series of events occurs after complete removal of the liver tissue and a collection of data has been begun with regard to the changes which take place in the organism during the period the animal appears normal.

The data so far obtained do not justify many positive statements of the events after the removal of the liver or the cause of death.

There seems to be some change in metabolism whereby some intermediate toxic product is produced or some necessary element for metabolism is lacking. The process is probably of the same general nature, although of somewhat different characteristics than that following the removal of the adrenals or the parathyroids.

Special observations were recorded in a few cases:

1. One animal was transfused with blood and saline solution shortly after the first symptoms were noted. The usual course of the reaction did not seem to be affected by this procedure.

2. One animal was fed on a diet of liver for two weeks before the final operation. Except that the convulsions were more marked the results did not differ from those in other animals.

3. In two animals the carbon dioxide combining power of the plasma was estimated just before operation and again after the onset of the moribund condition. In both instances it was initially rather high and decreased slightly after operation, but not enough to account for any of the symptoms.

4. In one animal blood creatinin and in two animals urea determinations made before operation and during coma yielded normal values.

5. While careful estimates of the clotting time of the blood have not been made, gross observations have not revealed any difference. In one experiment blood removed just before death clotted in six minutes.

6. In two experiments in which observations were made bile appeared in the urine and in the plasma after operation; it was not present before operation.

7. In three animals the urine was tested for sugar after operation; sugar was found in one, but it disappeared before death.

8. In one experiment the blood sugar was estimated at various periods after operation. It progressively decreased to less than half its normal value.

Summary. A method is described for the total removal of the liver of a dog without complicating factors other than the anesthetic. This makes it possible to study the effect resulting solely from the loss of liver tissue. An animal from which the liver is removed by this technic recovers from the immediate effects of the operation and then presents a definite and characteristic syndrome, a sequence of events invariably ending in death. The length of life after removal of the liver in this series of experiments has been from five to eleven hours.

ALIMENTARY HYPERSECRETION; GASTRIC HYPERSECRETION; GASTROCHRONORRHEA.

By Burrill B. Crohn, M.D.,

and

Joseph Reiss, M.D.,

new york.

(From the Pathological Laboratory and the First and Second Medical Services of the Mount Sinai Hospital, New York City.)

We are in the midst of a period in clinical gastric research wherein the attention of the majority of workers is focussed on diseases characterized by organic or structural changes in the tissue wall of the stomach or duodenum. Ulcer and cancer are the all-absorbing topics of discussion, and not without good reason. The advent of the roentgen ray, with its marvellous ability to portray defects and distortions of the borders of the organ, has given a strong impulse to the study of structural diseases. In so doing the observations of functional disturbances have fallen into the background and a lesser interest and eagerness have been shown in attempting to reclassify and evaluate the various forms of secretory disturbances to which the stomach, as a major secreting organ, is subject.

The total daily gastric secretion is no inconsiderable factor in the human physiology. It is estimated in amount as normally up to 1000 c.c., being thus second only to that of the kidney, though in composition its excretion is much more simple and chemically less complex. The older methods for the study of this secretion lay entirely in the use of the single test-meal, be it Ewald, Riegel, Sahli or other. Such a method was inadequate and unsatisfactory and contributed much to the lack of interest in the functional gastric diseases.

The introduction of a newer and improved method for withdrawing specimens of stomach secretion, the fractional test-meal, has given us an opportunity to look back over some of the older though still mooted questions in gastro-enterology in the hope that the application of such a method would throw a new and elucidating light on disputed points still far from settlement.

The topic of hypersecretion is just such a one. It has remained to date still a point in debate as to whether gastric hypersecretion was a normal phenomenon or whether it was a purely nervous phenomenon or whether after all hypersecretion was a manifestation of ulcer. Boas,[1] as recently as 1911, says that the significance of this phenomenon remains with future students to interpret, and though frequently expressing his personal

opinion in a discussion of the facts, always guards himself against some future reversal of his stand on any point.

Since Reichmann,[2] a practising physician in Warsaw in 1882, first described a case which he called "Magensaftfluss," up to quite recently, a prodigious amount of energy and effort has been spent in attempting to elucidate the clinical and chemical picture which he presented. Reichmann described a single case characterized by the presence in the fasting stomach of a large amount (100 to 1000 c.c.) of a fluid, bearing all the properties of pure gastric secretion. Clinically the patient suffered from progressive emaciation, headaches, vomiting, pyrosis, eructations and postprandial pains, particularly severe at night. Reichmann regarded his case as a functional secretory overactivity of the gastric glands; six hours after a full meal he was able to remove by lavage two and a half liters of gastric contents, containing food, sarcinæ, yeast and much hydrochloric acid. He does not suggest the possibility of ulcer nor does he mention ulcer as a possible factor underlying the complaint.

His publication aroused much discussion and brought out many publications, among the most important of which were those of Jaworski and Glucinski,[3] Riegel,[4] Schreiber,[5] Rossbach,[6] Jurgensen[7] and others. The discussion hinged mainly on the point whether Reichmann had described a rare and very unusual condition or whether hypersecretion was not, at least in its milder grades, a rather common clinical phenomenon. The dispute centered mainly upon the amount of fasting contents that could be called normal. Rosin,[8] Riegel,[9] Martius[10] and Strauss[11] found in the normal fasting contents not over 12 to 20 c.c. of fluid. Boas,[12] Huber[13] and particularly Schreiber[5] found normally up to 50 and 100 c.c. These authors, being unable to agree upon an accepted maximum figure for the amount of fasting contents, were unable to agree as to what to call hypersecretion and what to call normal. Riegel,[9] who believed that the normal fasting stomach should be nearly empty, found many cases which he regarded as mild hypersecretion, while Schreiber,[5] whose normal standard was much higher, regarded real hypersecretion as excessively rare. Jaworski[14] found the condition present in 115 of 159 cases examined. In 1887 Reichmann[15] contributed a more complete study of the syndrome he had originated. He described many cases in which the phenomenon occurred periodically, attributing the findings to various conditions of nervous irritability such as tabetic crises, hysteric crises, etc., but was able to collect in these five years only six real cases wherein pure continuous hypersecretion occurred, independently, in his opinion, of any organic lesion.

From this time to the present the discussion continues as to the occurrence of the disease as a clinical entity and as to the interpretation of continuous hypersecretion when it does occur. In general it may be said that differ as they might on the incidence of the

disease, nearly all agreed that hypersecretion was a symptom of functional overstimulation of the gastric glands through excessive nervous excitation.

The advent of the period of gastric surgery introduced an entirely new and very valuable factor. The increasing recognition of gastric and duodenal ulcer as an etiologic factor in abdominal disorders caused a reclassification of diseases of the stomach. One notes, particularly in this field, the swing of the pendulum in favor of organic explanations, Soupault[16] operated upon 58 cases of so-called gastrosuccorrhea and reported finding ulcer in all. Hayem[17] and Mathieu,[18] leaders of the French school of gastro-enterologists, accepted this view with few reservations. Boas[1] in the 1907 edition of his book was undecided, but in the 1911 edition he attributes at least two-thirds of the cases to gastric or duodenal ulcer though admitting the existence of some of the cases upon a purely neurotic basis. Ewald,[19] however, still clung to his opinion of a real neurosis as the basis of the phenomenon.

Interest in the subject of the milder forms of hypersecretion as one phase of the gastric physiology of digestion was actively renewed when Strauss,[11] in 1903, pointed out the very common occurrence of hypersecretion in numerous gastric disorders. Strauss, and those that took sides in the discussion which he aroused (Zweig, Calvo, Huppert, Grandauer), laid little emphasis on the amount of fasting contents. They described "alimentary" hypersecretion, that is, an excessive digestive secretion occurring during and after the period of active digestion. To them "Reichmann's disease," or continuous hypersecretion, was a rare and much exaggerated form of alimentary hypersecretion. In its milder form it occurred in 31 per cent. of all male cases, and 8 per cent. of all the female cases examined. These authors were divided as to its interpretation; the weight of opinion, however, favored hypersecretion as being a state of increased secretory stimulation, in the largest percentage due to ulcer or other intrinsic gastric causes.

This rather prolonged review of the literature should be pardoned by the reader. There is so much of confusion associated with the phrase "gastric hypersecretion" that it has been deemed not superfluous to collect the opinions of those who have previously been interested in this topic. Summarizing these efforts, one distinguishes the following:

A. *Continuous Hypersecretion* (Magensaftfluss or Reichmann's disease), a malady having a characteristic clinical picture and evidenced by continuous outflow of large quantities of secretion both in the digestive and interdigestive and fasting states. Surgery has pretty nearly classified most of these as cases of pyloric stenosis due to ulcer; the medical men succeeded in establishing a smaller number on the basis of pure neurosis.

B. *Continuous Hypersecretion*, occurring not chronically but in intermittent form, associated with periodic migraine, tabetic crises,

paroxysmal hysterical vomiting spells, etc. These are accepted by all as cases due to excessive stimulation of the gastric nerves of central nervous system origin.

C. *Alimentary Hypersecretion*, not really a disease but a symptom or chemical phenomenon occurring during digestion. This milder form of secretory stimulation was shown to be a very common phenomenon and generally attributed to protopathic organic origin, usually ulcer.

The fractional test-meal as a means of studying gastric physiology and chemistry, having introduced a new and undoubtedly valuable clinical method, it has been deemed warrantable to reopen this subject for investigation. The Ewald test-meal furnished information of the activity of the stomach at its supposed height or one hour after the ingestion of a simple meal, but it can readily be shown that hypersecretion when it does occur, takes place almost entirely after the fastigium is reached or in the declining stage of motor activity. The very definition of magensaftfluss or gastrochronorrhea (Hayem) is secretion activity after the digestive cycle and in the interdigestive cycle. Hence the fractional method has furnished an ideal means for studying the digestive, postdigestive and interdigestive states. In so doing it has established an entirely new criterion upon which to base the judgment of what is or what is not a normal amount of gastric secretion, and what is the clinical significance of an outflow of digestive juices when it occurs to an abnormal degree. In fact, Hayem[20] who years ago used repeated test-meals, extracting them on successive days, one-half, one, one and a half, and two hours after ingestion, introduced the term gastrochronorrhea as an improvement on the term gastrosuccorrhea to indicate an abnormal secretion in the post and interdigestive periods. When discussing this disease his attention was entirely focussed on this phase of the subject.

In the fractional test-meal as at present employed, with the indwelling tube of Rehfuss, and using oatmeal gruel as a test substance, it is simple to determine the amount of secretion poured out by the secretory acini in proportion to the residue of gruel in the stomach at any given period.

The fasting stomach contents being first removed and the gruel meal being drunk, successive fifteen-minute specimens are withdrawn until no further material can be aspirated. The first quarter of an hour specimen is normally nearly all gruel, or at least four-fifth gruel and one-fifth secretion. At the end of the half-hour there is still at least two-thirds gruel and one-third secretion present. By the end of the first hour the stomach has produced about as much secretion as there is gruel in the viscus, always remembering, of course, the fact that gruel is constantly passing out of the stomach through the pylorus. In the successive periods the secretion becomes relatively more abundant and the gruel less in amount, until by the sixth or seventh quarter-hourly specimen there is only one-sixth to

one-eighth of gruel present in the test-tube, upon settling, all the remainder being secretion produced by the glands. At the end of one and three-quarters to two hours the stomach has expelled the last trace of gruel (iodin-starch test negative). Normally the glandular secretion ceases after this period and further attempts to aspirate either meet with no success or bring up only two or three c.c. of mixed gastric mucus and saliva. The stomach as a secretory digesting organ has come to rest. If the secretion of the stomach, now more properly called parasecretion (Boas), continues we have the phenomenon of hypersecretion or supersecretion. This hypersecretion may be present during the latter stage of the normal digestion, as evidenced by the greater proportion of secretion to gruel in the withdrawn specimens; and it may and usually does last for one-half to one hour after the organ has completely evacuated the food. This we recognize as alimentary hypersecretion. If the parasecretion is present during the second, third and fourth and later hours of the postdigestive cycle we recognize a continuous hypersecretion, or gastrochronorrhea.*

The following original studies have been made upon 50 cases in which sixty-eight fractional tests have been made. The cases were collected in the medical wards of Mount Sinai Hospital, a smaller percentage being added, from the private practice of the writers. Clinical observations were maintained for a period in each case of several weeks; in many of the cases the observations extend over months and in some years. Careful clinical and chemical studies, exact roentgenologic observations, and in many cases findings at the operating table tend to form as complete a collection of data as is possible, upon which to base a diagnosis of the underlying condition. Cases in which a definite and marked delay in motility was present have been excluded particularly if food residue or sarcinæ and lactic acid were present in the fasting contents, as these cases were evidently examples of pyloric stenosis of organic origin and not simple hypersecretion. In these cases there being practically no interdigestive state but just one continuous stage of digestive activity, we are unable to judge of the condition of the organ in the usual resting period.

Incidence. It is impossible to judge of the frequency of the occurrence of hypersecretion in the hospital, as no statistics have been kept of the total number of fractional test-meals taken. At Mount Sinai Hospital the fractional test is employed almost as a routine test; the number of observations is therefore very large. An idea of the incidence of hypersecretion is more easily judged from the cases seen in private practice. Of the last 100 fractional tests taken in the office by the authors twenty showed definite hypersecretion (20 per cent.). This figure is lower than that of Jaworski,[14] who found 115 instances in an examination of

* Strauss,[11] using a test-meal of dry crackers, recognizes a percentage of dry residue to secretion greater than 1 to 4 or 5 as a case of hypersecretion.

159 patients. (As was previously noted, Jaworski judged almost entirely on fasting content findings.)

As a symptom, hypersecretion is anything but rare, When Reichmann[2] first described the syndrome it was regarded as unusually uncommon. The later writers, as well as these figures, prove it to occur in at least 1 out of every 3 cases examined.

Sex. The male sex predominates greatly, 88 per cent. of the cases being in males. This agrees with the data of the older investigators.

Age Incidence. There are no observations below the ages of twenty and none over seventy years. Approximately 55 per cent. of the cases occurred between thirty and fifty years of age, 16 per cent. between twenty and thirty years.

Seasonal variations are not noticeable.

Laboratory Data. In cases of hypersecretion the fasting contents of the stomach is increased. It is useless to enter into a discussion as to the maximum amount of secretion found in this viscus in the morning before the first meal has been taken (*liquid à jeun*). Estimates of various authors show a wide range, most of them lying between 10 and 20 or 30 c.c. However, many other writers include any amount up to 50 to 100 c.c. as normal. These latter figures are too high in our experience. The fasting content in many hundreds of cases is normally rarely more than 30 c.c.; larger amounts indicate abnormal secretory activity or delayed motility, or both. In this series of 50 cases of hypersecretion the resting stomach in the morning contained on an average 65 c.c. The actual figures lie between 0, found only once in a case of achylia with hypersecretion, and 180 c.c. in a case of ulcer with normal range of acidity but marked hypersecretion. Findings of 90, 120, 130 c.c. or more are common. The fluid withdrawn is always clear, watery, slightly milky or cloudy and shows a faint admixture of bile and salivary secretion. Food residue is never present in cases of pure hypersecretion without organic pyloric stenosis. The fluid found is practically a pure secretion of the gastric tubules. We have been fortunate enough to observe 2 cases in which we could prove an active secretion in the fasting case. In 1 of these cases 130 c.c. of pure watery secretion was removed. After five minutes another 30 c.c. of clear aqueous liquid was extracted, and thereafter every five minutes 30 c.c. of the same liquid clear material was aspirated. This was observed for a half hour, whereupon our observations ceased, though the fluid was still being produced. The material withdrawn was free of biliary and pancreatic regurgitation, as evidenced by its color and freedom from pancreatic ferments, and free of saliva, the patient being watched and instructed to expectorate all fluids accumulating in the mouth. In this case at least a definite rate of flow was observed; 30 c.c. every five minutes, or 360 c.c. an hour. If continued for twenty-four hours in the fasting state this

would have meant 7344 c.c. per day. During the digestive periods this rate of flow would probably have been much accelerated.

We have attempted to collect fasting secretion in many patients not suffering from hypersecretion, by similarly emptying the residue and then watching every five minutes for evidence of normal secretory activity, but could never collect more than 1 or 2 c.c. of viscid material in such an interval.

The acidity of the fasting contents in hypersecretion shows the same range as normal cases, free acid ranging from 0 to 94 per cent., average 30 per cent.; total acidity from 10 to 100 per cent., averaging 52 per cent. The acid titer of the fasting stomach is usually lower than the acidity at the height of digestive activity, but is usually of the same titer as is the fluid produced in the postdigestive hypersecretory phase. The titer of the fasting contents is the titer of the gastric secretion of that individual stomach for the whole of the twenty-four hours except for the short periods in which digestive activity is at its maximum.

Ewald Test-meal. The most important factor to be determined is the total amount withdrawn. This varied between 10 c.c. (achylia gastrica) and 325 c.c. as a maximum. The average amount was 102 c.c., a figure decidedly above the normal. The proportion of fluid to solid food residue (starch) was always from 4 to 1 to 10 to 1, indicating a large increase in the secretory quotient. The acidities were for free acid an average of 35 per cent., for the total acid 64.3 per cent.

Fractional Test-meals. It is with the fractional test that the greatest information is derived. The curves were observed (quarter-hourly) for from two to six hours, after the ingestion of the gruel. As the emptying time was not materially different from the normal standard, practically every period after two hours (or two and a quarter hours) represents a pure hypersecretory phase. The duration of the observations in most of the cases was limited only by the time at the convenience of the observer and the fortitude and indulgence of the patient. Most of the cases observed four, five and six hours were secreting just as strongly then as at the beginning and gave every indication of being cases of continuous hypersecretion. On the other hand, after the two- or three-hour period some of the cases seemed to wane, and some to come to an end, with a gradual fall of the acidity curve. These were examples of alimentary hypersecretion. Between 50 per cent. and 60 per cent. of the cases gave every indication of being of the continuous type. This is a rather striking figure in contrast with the idea of Reichmann, Riegel and others, who regarded continuous hypersecretion as a very rare phenomenon. It is probable that some or many of the cases regarded here as alimentary would also have fallen into the class of continuous secretion had they been observed for a longer period.

The maximum height of free acid in this series of fractional tests

ranged from 0 to 114 per cent., but averaged 69.2 per cent. The maximum titer for total acidity varied from 14 per cent. or 20 per cent. in very few cases, to 140 per cent. in extreme types. The average for all cases was 84 per cent., but the number of cases titrating between 100 and 136 was 16 out of a total of 68 curves studied. From these figures we readily surmise that hyperacidity and hypersecretion are close concomitants, though not necessarily so. The type of the curve is of more interest than the height or altitude of acidity reached. The curve in most cases shows two phases: a primary or digestive phase, following rather closely the usual digestive curves and showing a tendency to return toward the base line at the end of two hours (emptying time); and a secondary curve, characterized by a slight secondary rise until a certain level is reached. This level is maintained with very little variation for hours and hours. The level sought by any individual is personal to that individual; some stand steady at 40 per cent. for total acidity, some at 50 per cent. or 60 per cent. and a few still higher. Such an illustration is seen in Chart I, representing a case of pyloric ulcer with a mild grade of pyloric stenosis present. The secondary phase is established at 50 per cent. acidity.

Pathologic physiology has emphasized the supreme importance of motility and emptying time in the stomach.

In cases of pure hypersecretion without evident organic disease there is no change from the normal standard of motility. Occasional exceptions will be noted later. The presence of a pyloric or peripyloric ulcer introduces another and a mechanical factor, often coexistent with the hypersecretion. In the presence of organic disease, delay in motility can safely be attributed to the pathologic process. In a large number of this series where no organic disease was suspected a normal emptying time existed in the presence of marked hypersecretion.

The Clinical Diagnosis in Cases of Hypersecretion. The cases in this series were grouped under the following diagnoses.*

TABLE I.

Duodenal / Gastric } ulcer	13
Carcinoma of stomach	3
Carcinoma of common bile duct	1
Cholelithiasis	2
Gastric neurosis	19
Syphilis, tertiary	3
Syphilis, tabetic crises	1
Migraine, neurosis	2
Spastic colitis, neurosis	2
Asthma	1
Achylia gastrica	1
Chronic appendicitis	5
Tuberculosis of kidney	1

* In four of these cases a diagnosis of concurrent duodenal ulcer and chronic appendicitis is made.

It is readily observed that hypersecretion is a symptom, common to many diseases and conditions, and pathognomonic of no single one.

In order the better to appreciate the factor of hypersecretion in the various types of maladies let us consider a few illustrative cases with their corresponding chemical data.

Chart I illustrates the fractional curve of a case of pyloric ulcer with a moderate degree of organic pyloric stenosis. The patient, an adult, male, aged forty-five years, had suffered epigastric cramps for two years. All food produced abdominal discomfort, eventuating in cramp-like pains one and a half to two hours after eating. Nausea and repeated vomiting supervened during the last five months. The fasting contents of this patient amounted to 130 c.c., no food residue being present. One hour after an Ewald test-meal 200 c.c.

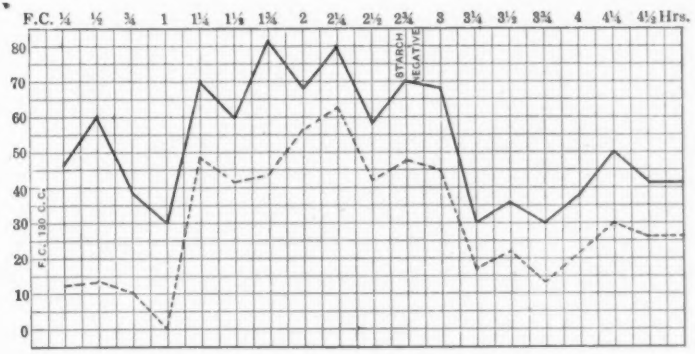


CHART I

were removed, having a free acidity of 55 and a total acidity of 88 per cent. Vomiting of large amounts of food was observed, up to 1000 c.c. being noted on one occasion. At operation a hypertrophied and thickened pylorus was palpated, adjacent to which was a large inflammatory mass adherent to the head of the pancreas.

The curve of this fractional test was typical both of a gastric or pyloric ulcer and of hypersecretion. The rise of acid was gradual and sustained reaching its height only at the one and three-quarter hour period and sustained to the third hour. The last trace of starch left the stomach at two and three-quarter hours, a definite delay from the normal. Subsequent to this emptying of the stomach there was a fall of acidity to a level of 40 to 50 per cent. total acidity, at which point the hypersecretion continued indefinitely; this supersecretion consisting of clear watery fluid continued uninterruptedly up to the last observation which was made five and one-quarter

hours after the ingestion of the oatmeal gruel. We observe here a prolonged and sustained digestive cycle with a maximum acidity between 70 per cent. and 80 per cent. and a secondary stage of supersecretion lasting indefinitely thereafter, though maintained at a constant though lower level of acidity. This case may well have been accounted as one of Reichmann's disease, for it bears all the clinical characteristics of such, as, for instance, abdominal pain, acid eructations, vomiting of very large amounts of fluid, loss of weight, excess of material in fasting contents and continuous secretion of the stomach at all times throughout the day.

Yet it was a case proved at operation to be one of peripyloric ulceration.

Chart II is an illustration of an instance of exaggerated hypersecretion, accompanying most likely a gastric or duodenal ulcer.

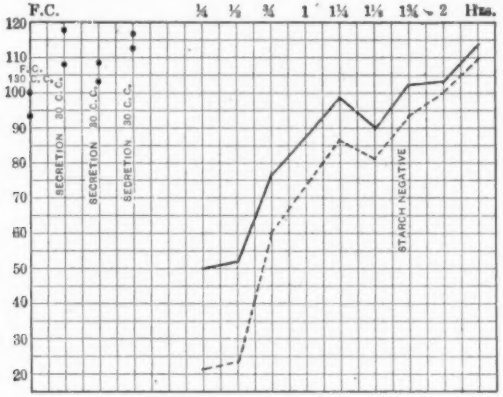


CHART II

During the last two years the patient had suffered with recurrent attacks of belching, heartburn eructations and constipation. The attacks were separated by intervals of three to five months of well-being. During the attacks copious vomiting took place, usually a few hours after eating, the vomitus being occasionally brownish-black in color. Stools were dark brown, but never absolutely black. On one occasion we were able to wash from this man's stomach skins of prunes eaten thirty hours previously.

The fractional chart shows that 130 c.c. fasting contents containing food were obtained. Thereafter (still in the fasting state) every five minutes 30 c.c. were removed, consisting of clear watery fluid and representing pure continued secretion in the fasting state. The gruel test-meal followed and demonstrated a condition of marked hypersecretion. The last gruel left the stomach at the

one and three-quarter hour period; following this we note another period of continuous gastrosuccorrhea, the observations being interrupted by the fatigue of the patient. The level attained by the gastric supersecretion was unusually high, reaching between 120 per cent. and 130 per cent. at the last observation.

We note that the level of acidity in this case in the empty or supposedly resting state is far different from that in the preceding one (Chart I), the resting level here being about 120 per cent. while in the previous one it is 40 to 50 per cent. We have observed many cases of ulcer in which the level of the supersecretion lay between these two extremes. The height or average altitude of acidity is no index of the disease and no level can be said to be characteristic of ulcer. Every person may be said to have his or her average level, common to that person both in health and disease.

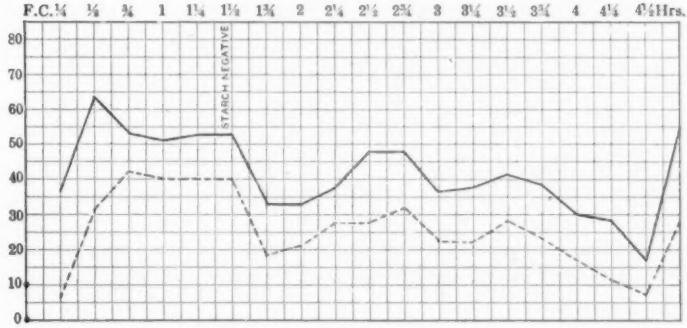


CHART III

The following case was one of a neurotic nature, with some evidence of mild disease process in distal organs. He suffered from an inactive pulmonary tuberculosis; he had complained for eight years of vague generalized abdominal pains and occasional attacks of diarrhea. He was of a neurotic temperament, easily frightened and irascible. A simple chronic granular proctitis and sigmoiditis was present. His gastro-intestinal roentgen-ray examination was negative. The chart (Chart III) of this case was typical of a continuous hypersecretion with low, titrable acidity; the primary digestive phase lasted only one and a half hours and was followed by a typical secondary continuous supersecretion lasting up to four and three-quarter hours, the observation being interrupted because of the fatigue of the patient at this point.

Chart IV illustrates the fractional curve in the case of an adult male suffering for four weeks from nervousness, sleeplessness, heavy

sensation in abdomen, loss of appetite and constipation. This was evidently an example of psychoneurosis with some abdominal symptoms. The chart was one of typical hypersecretion, there being a constant outpouring of abundant clear fluid in all the fractional tubes examined. Motility was normal.

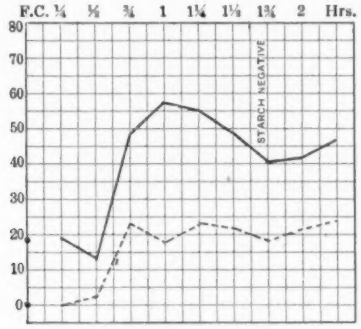


CHART IV

The hypersecretion present here was probably part of a general neurosis; hyperstimulation of the vegetative nervous system was manifested in many of his clinical symptoms.

The next case (Chart V) was that of a man, aged sixty-seven years, who had been under observation in the hospital on and off during

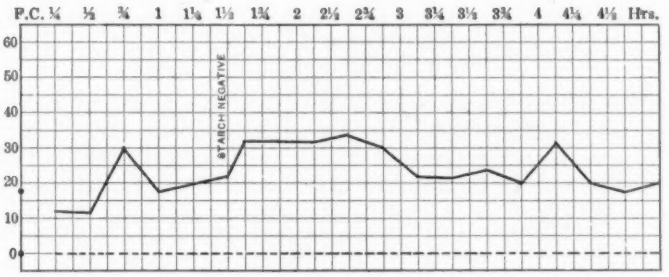


CHART V

the last five years, suffering from constant pain in the epigastrium referred to the precordium, worse in the fasting state. Generalized pruritus was present, as well as chronic constipation.

Chart V showed a condition of anacidity accompanied by a marked hypersecretion. The emptying time was one and a half

hours, yet when observed up to the four and three-quarter hour period this stomach was freely secreting a limpid fluid containing no free acid and a total acidity about 20 per cent. Only a few cubic centimeters of fasting contents could be obtained in the morning. There was present in this man a functional disturbance of the gastric secretion probably of a neurogenic origin.

Chart VI represents a similar case in a middle-aged female, with exaggerated subjective gastric symptoms. Thorough observation over several weeks failed to reveal the presence of organic disease. The fractional curve was one of complete anacidity (ferments faintly present) with a prolonged hypersecretion.

It is impossible to differentiate in such a curve the hypersecretory from the digestive phase.

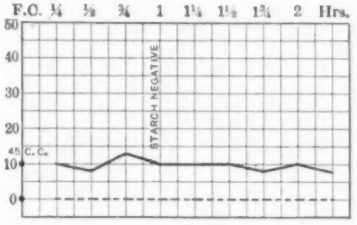


CHART VI

Cases 2 to 6 inclusive are examples of gastric neurosis with functional hypersecretion. The emptying time was normal in all, the range of acidity from complete anacidity to hyperacidity. Hypersecretion is the one common factor being present throughout, independent of the range of the acid titer. Vomiting was not present in these cases, nor were any large amounts of fasting contents obtained on repeated examinations. They are more in the nature of alimentary hypersecretion (hyperpepsia of Hayem) though some of them partake also of the character of continuous supersecretion (gastrochronorrhea of Hayem).

The next example is illustrative of a case of late syphilis, with 4-plus positive Wassermann reaction. Organic disease of the stomach was lacking, radiograms showing only ptosis with normal gastric contour. The Wassermann reaction in the spinal fluid was similarly 4-plus, though no clinical evidence of syphilis of the nervous system was present. The fractional curve, Chart VII, was typical of that of continuous hypersecretion; emptying time normal two and a quarter hours, followed by an enduring phase of pure hypersecretion observed up to four and a quarter hours.

Syphilis was present in 4 of the 50 cases studied and was an important factor etiologically.

The following 2 cases, Charts VIII and IX, were instances of general neurosis, accompanied by chronic migraine and frequent attacks of vomiting, often of large amounts of fluid. The malady extended in both cases over a large number of years.

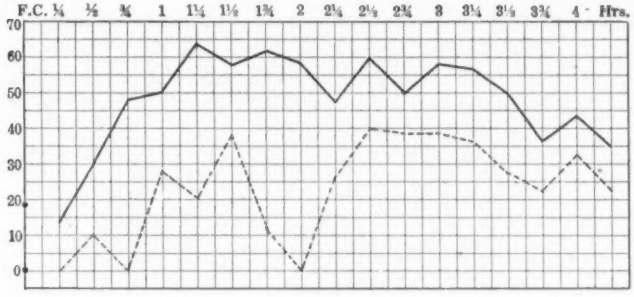


CHART VII

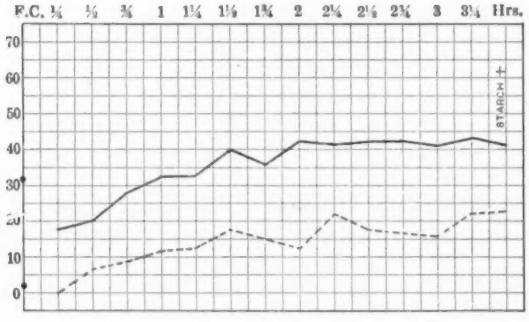


CHART VIII

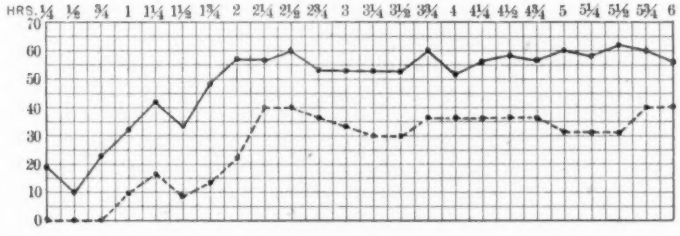


CHART IX

A definite delay in motility was observed in both cases. In Chart VIII we note that at three and a half hours starch (oatmeal

gruel) was still present in the stomach; in Chart IX starch was visible *at the end of six hours.* In this latter case organic disease at the pylorus was so strongly suspected that operation was advised. Laparotomy revealed a patent pylorus, easily admitting two fingers and no evidence of organic malformation. In this group we have hypersecretion accompanying the symptom-complex of migraine and associated with a definite delay in gastric motility. Pylorospasm is here probably the primary gastric factor, the hypersecretion being due to the prolonged stay of the food in the viscus.

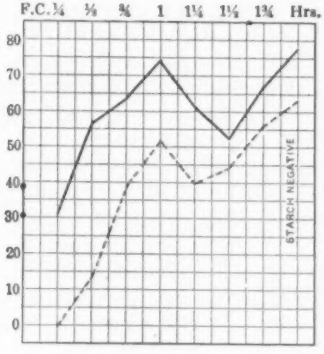


CHART X

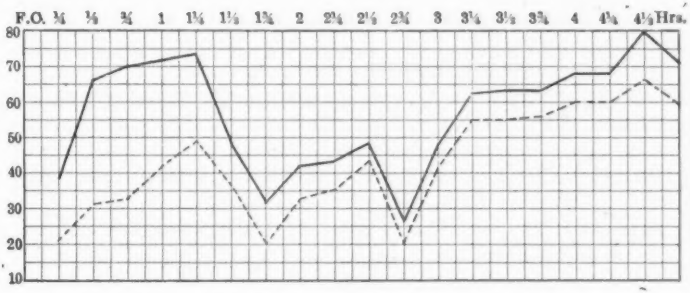


CHART XI

What relationship exists between hypersecretion and the various clinical pictures with which it is associated? A reference to Table I will show that it is associated with no single clinical complex or disease. It exists as a frequent concomitant of gastric and duodenal ulcer, more particularly of the former. As such it is often associated with delayed motility due to pylorospasm or pyloric stenosis (5 out of 13 cases), while in another larger group (7 out of 13 cases) motility was normal and yet hypersecretion present.

If to this group we add the 3 cases of carcinoma of the stomach with hypersecretion, we have 16 cases of gastrosuccorrhea apparently due to protopathic or intragastric irritative stimulation. Many of these cases were rather typical of the syndrome of Reichmann's disease as he first described it in 1882. It is quite probable that in the early literature all cases of Reichmann's disease were cases of pyloric ulcer or pylorospasm from gastric or duodenal ulcer. Among these 16 cases of organic disease of the stomach is a fair number showing only limited degrees of hypersecretion (alimentary hypersecretion) and not developing at any time the *continuous* magensaftfluss and copious vomiting of the Reichmann syndrome. Further we know from our own statistics published in an earlier paper[21] that only 30 per cent. of all gastric or duodenal ulcers show hypersecretion. Thus we may draw the conclusions that organic disease of the stomach (ulcer or neoplasm) explains only about one-third of the cases of hypersecretion.

In the next group we can place 2 cases of cholelithiasis and 3 cases of chronic appendicitis, all with reflex gastric symptoms. These form a very well-defined group. In the 3 cases of chronic appendicitis, with irritative symptoms perfect health and function was restored after the removal of the appendix. These 5 cases, together with a case of carcinoma of the common bile duct, constitute 6 cases of organic disease in neighboring organs with reflex gastric hypersecretory phenomena.

The type of curve in these cases was more in the nature of alimentary hyperpepsia than modelled after the chronic supersecretive type. This group represents extrinsic gastric stimulation of organic and abdominal origin.

The remaining cases fall into a final group. They produce their irritative hypersecretory phenomena through the nervous regulatory apparatus of this important secretory viscus. There seems little doubt that psychical influences play an important role in many of these cases. Thus in two of the cases included in this series, "bad news" initiated the subjective gastric phenomena.

In another case, one in the hospital ward being treated for asthma, an interesting observation was made. He was a young male adult suffering for many years with attacks of asthma occurring at irregular intervals. He complained, in addition (during the last four months), of severe abdominal cramp-like pains in the right hypochondriac region, referred to the back. Vomiting occurred on an average of once a week and gave relief from subjective symptoms. Heartburn set in usually fifteen to thirty minutes after a meal.

During the earlier part of the stay in the hospital the asthma was not severe, in fact almost unnoticeable. The patient was given a Sippy diet in an attempt to control subjective gastric symptoms.

The curve before instituting the diet showed a rising and sustained curve, slight hyperacidity, motility normal. During the

first ten days of restricted diet the patient reported progressive improvement; on the tenth day the patient became excited over the administration of a dose of Epsom salts for constipation. He felt convinced that the cathartic had harmed him and injured his treatment. During his excitement a severe attack of asthma set in. A fractional test which had been ordered for the same morning showed a marked hypersecretion of the most typical continuous type (magensaftfluss). Specimens were obtained up to four and three-quarter hours after the ingestion of the meal and the profuse limpid fluid flowed freely.

This incident is cited to indicate the role that powerful psychic irritation plays in the control of secretory regulation in the body. Pawlow and Cannon have emphasized the influence of fear, anger and other excited emotions on the gastric secretions. In the experimental studies on animals inhibition of secretion was more common. In this clinical case there is evidently a direct central nervous system stimulation with apparent radiation down the stimulatory fibers of the vagus, inducing probably both the asthma and the gastric hypersecretion (parasympathetic path).

It is comprehensible that most of the cases in the group of "neuroses" bear an analogy to this the above incident. For in them there is a constant nervous overexcitation. Bad news from home or an irritating incident serves only to exaggerate the type of the case.

Organic nervous disease may and does cause the same symptoms. Tabes has long been recognized as an etiologic factor in periodic gastrosuccorrhea (von Leyden). Tumor of the brain may do the same as well as hysteria. This is the group classed by Reichmann and accepted by successive writers as "periodic continuous hypersecretion," that is hypersecretion present during the attacks or crises of the nervous malady and absent in the remission periods. The clinical picture termed by Rossbach "gastroxynsis," is only another subspecies of this same group; it consisted of attacks of vomiting of copious amounts of fluid associated with headache and crises of nervous or hysteric character.

The curves obtained in the cases of migraine were remarkable not only for the presence of hypersecretion but because of the very prolonged emptying time of the organ. There is evidently a powerful nervous stimulus irradiated along both motor and secretory nerves of the organ, inducing motor pylorospasm and secretory hyperstimulation. As a clinical picture pylorospasm as a result of organic disease of the central nervous system is well recognized as an accompaniment of tabes, brain abscess or brain tumor. The stimuli reaching the stomach in the above-cited cases of migraine are apparently of analogous, though not identical origin. We have established hypersecretion as occurring then, in three groups of cases:

1. Organic disease of the stomach, particularly ulcer (intrinsic origin).

2. Organic disease of associated abdominal organs (reflex action).

3. Hyperirritable conditions of the cerebral or autonomic nervous system, both organic or psychic (extrinsic origin).

Does hypersecretion ever occur in normal individuals? Rehfuss[22] has expressed the opinion that hypersecretion does occur occasionally in individuals in a state of perfectly normal health, and cites an instance in a group of students studied as normal controls. He reiterated this opinion quite recently in a paper[23] read before the American Gastro-enterological Society last year. Yet the large number of control cases cited by him in his series, as well as those of Fowler and Zentmire,[24] and our own controls, numbering many hundreds in hospital cases observed for all varieties of ailments, denies the point that hypersecretion is a normal phenomenon or occurs more than as a great exception in persons entirely devoid of organic or psychic stigmata. It is just as likely that the occasional so-called normal individual upon whom a control test is made is really a potential psychoneurotic or vagotonic. It may be argued that all of our studies have been on chronic hospital cases or cases actively complaining of well-defined symptoms. Still we answer that in the hundreds of cases observed with a functionally normal digestive organ the stomach empties itself promptly at two hours, and thereafter no further secretion is obtainable. All cases varying from this standard by showing digestive or post-digestive hypersecretion are regarded as suffering with a functional aberration from the normal secretory standard of health.

In the light of the studies made upon this series of 50 cases, closely observed and studied, let us review critically the clinical literature of the last twenty-five or thirty years on the subject of hypersecretion. Does Reichmann's disease exist today as an independent clinical entity? This is best answered in the negative. Practically all the cases described by Reichmann [2 15] and Riegel,[4 9] Strauss,[11] and others were typical instances of ulcer complicated by continuous hypersecretion. Soupault operated upon 58 cases of so-called Reichmann's disease and found ulcer in all of them.

But continuous hypersecretion as a symptom does exist, not as an independent disease but as one symptom, usually a secondary symptom, of other diseases, organic or neurogenic.

All the clinical symptoms of Reichmann's disease, such as pains, vomiting, pyrosis, loss of weight and continuous hypersecretion may be seen associated with various clinical conditions other than peptic ulcer.

The group of periodic hypersecretion stands today in an unmodified and strong position, as originally described by von Leyden,[25] Rossbach,[6] Moebius[26] and others. The hypersecretion is not the

disease but is the secondary phenomenon of a malady of the cerebral nervous system.

What can we say of digestive or alimentary hypersecretion, as revived by Strauss,[11] and discussed by Calvo and Zweig,[27] etc.? Many of these writers attempted to associate all hypersecretion with ulcer. We see from the data in this series of cases that they claimed too much and that barely a rough 33 per cent. can be so classified.

It may not be amiss to discuss the nervous mechanism by which an abnormal secretory activity of the gastric acini is produced. The stimulatory fibers to the glands of the stomach are regarded as being in the parasympathetic system or the pneumogastric nerve; inhibition of secretion rests with the sympathetic system whose neurons lie in the celiac plexus. The extrinsic motor control follows in general the same routes. Abnormal stimuli originating in other nervous ganglia of the abdominal plexuses are referred or reflected along the vagus system, producing exaggerated peristalsis, pyloric irritability and pylorospasm and supersecretion. This is termed by Head and Pottenger[29] a viscerosensory reflex. The close association between vagotonia (Eppinger and Hess[30]) and most of these cases of hypersecretion is worthy of attention. The relation of vagotonia to ulcer of the stomach and duodenum has been repeatedly pointed out (Petrin and Thorling[31]); one cannot overlook the possible sequence of vagotonia, hypersecretion and ulcer. Hypersecretion of long standing may conceivably induce ulceration, or, *vice versa*, the presence of an ulcer may cause, by intrinsic irritation, a sequential supersecretion.

The efforts of Nikolaysen[32] to produce hypersecretion by pilocarpin stimulation of the vagus nerve were unsuccessful; his experiments are too few to warrant sincerely doubting the above-mentioned hypothesis.

There is reason to believe that adrenal insufficiency plays a role in this symptom, either through the thyroid gland or independently of it. The experiments of Finzi,[33] of Friedman[34] and of Mann[35] in the production of ulcers by adrenalectomy and pilocarpin injections are very suggestive along this line.

The question has often been raised by previous writers whether delayed motility was not accountable for the large amounts of fasting contents and test-meals removed in this class of cases. J. Kaufmann[36] has demonstrated in a typical case of Reichmann's disease that the predominant factor was a delay in motility due to ulcer. There is no question that in the cases of gastrosuccorrhea of organic gastric origin, delayed motility plays an important and mechanical role. But in the remaining cases of this group, periodic and alimentary hypersecretion, no delay in the exit of food was demonstrable. Atony as a factor deserves today but little consideration, since normal emptying time is not inconsistent with a

well-marked atony. It is the opinion of the authors that delayed motility is not an essential or intrinsic factor in hypersecretion. It often accompanies gastrosuccorrhea, but just as often, or more so, we note normal emptying time with exaggerated supersecretion.

The cases of migraine with markedly delayed motility are exceptions, but deserve very close notice because of the unusual and extensive degree of the motor insufficiency.

Treatment. The indications for the treatment of gastric hypersecretion are clearly laid down in the general principles of this paper. The importance of removing both extrinsic and intrinsic stimuli of an abnormal nature is self-evident. Restriction of diet is one of the basic principles; rest in bed is a necessary corollary of this treatment. In a series of cases of hypersecretion studied by the author and previously reported the effect of marked restriction of diet, both solid and fluid, was studied; 45 per cent. showed local improvement in the chemism of the stomach and 80 per cent. were discharged from the hospital free of symptoms. The use of atropin is warranted by experiments published recently.[37] We were able to demonstrate a striking reduction in the supersecreted fluid after hypodermic administration of this alkaloid. Less favorable results followed the administration by the mouth or over even longer periods.

The removal of abnormal nerve stimuli, whether of cerebral nerve system or of viscerosensory origin, is self-evident; no treatment that ignores the psychical condition of the patient will be effectual in a case wherein vagatonia is a factor or hysteria or a psychoneurosis is present.

Organic brain or spinal-cord disease once diagnosed, calls for its own treatment.

Summary. 1. Hypersecretion is a symptom; it is a functional disturbance of the secretory apparatus of the stomach. It is not a disease *per se*.

2. It is a frequent symptom, occurring most commonly in males, and being present in probably at least 10 to 15 per cent. of all persons with gastric complaints.

3. Its occurrence is independent of the acidity titer of the stomach; it is found more often associated with hyperacidity, but can be seen through all the grades of acidity, even in achylia gastrica.

4. Most of the cases of hypersecretion are of the continuous type, lasting throughout the digestive and intergestive period. The most severe type of cases, when associated with vomiting, emaciation, thirst, epigastric pain, etc., constitute Reichmann's disease. These cases are nearly all due to gastric or duodenal ulcer (Intrinsic cause).

5. Of the milder grades of continuous hypersecretion (alimentary hypersecretion, without vomiting, etc.), many of the cases are attributable to ulcer (about one-third); the remainder are due to abnormal nerve irritation, either *reflexly* from abdominal disease in other organs or from neurotic instability, such as vagotonia, psychoneurosis, etc. (extrinsic cause).

6. A few cases are due to diseases of the cerebral nervous system, hysteria, psychic causes, etc. (intermittent hypersecretion).

BIBLIOGRAPHY.

1. Boas: Diagnostik und Therapie der Magenkrankheiten, 1911, p. 506.
2. Reichmann: Berl. klin. Wchnschr., 1882, xix, 606.
3. Jaworski and Glucinski: Ztschr. klin. Med., 1886, xi, 50, 270.
4. Riegel: Deutsch. med. Wchnschr., 1892, xviii, 67.
5. Schreiber: Deutsch. med. Wchnschr., 1893, xix, 692.
6. Rossbach: Deutsch. Arch. klin. Med., 1884, xxxv, 383.
7. Jurgensen: Deutsch. Arch. klin. Med., 1888, xliii, 9.
8. Rosin: Deutsch. med. Wchnschr., 1888, xiv, 966.
9. Riegel: Deutsch. med. Wchnschr., 1893, xix, 735.
10. Martius: Deutsch. med. Wchnschr., 1894, xx, 638.
11. Strauss: Mitth. a. d. grenz. Med. u. Chir., 1903, xii, 25.
12. Boas: Diagnostik und Therapie der Magenkrankheiten, 1911, p. 503.
13. Huber: Corresp. aus Schweitzer Aerzte, 1894, vol. xix.
14. Jaworski: Wiener med. Wchnschr., 1886, xlix, 52.
15. Reichmann: Berl. klin. Wchnschr., 1887, pp. 199, 221, 240, 282.
16. Soupault: Traité des Maladies de l'Estomac, 1906, p. 303.
17. Hayem: Les Evolutions Pathologiques de la Digestion Stomacale, 1907.
18. Mathieu: Traité Medico-Chirurgical des Maladies de l'Estomac et de l'Esophage, Mathieu, Lencert and Tuffier, 1913.
19. Ewald, C. A.: Diseases of the Stomach, 2d ed., 1897, p. 501.
20. Hayem and Lion: Nouveau Traité de Médecin, Maladies de l'Estomac, 1913.
21. Crohn and Reiss: Am. Jour. Med. Sc., 1920, clix, 70.
22. Rehfuss: Jour. Am. Med. Assn., 1914, lxiii, 11.
23. Rehfuss: Tr. Am. Gastro-Enterological Society, 1919, p. 58.
24. Fowler and Zentmire: Jour. Am. Med. Assn., 1917, lxviii, 167.
25. Von Leyden: Quoted by Boas.
26. Moebius: Quoted by Boas.
27. Zweig and Calvo: Arch. Verd., 1903, ix, 263.
28. Head: Brain, 1893, xvi, 1, etc.
29. Pottenger: Symptoms of Visceral Disease, 1919, p. 16.
30. Eppinger and Hess: Vagotonia, 1917, 2d ed.
31. Petrin and Thorling: Ztschr. klin. Med., 1911, lxxiii, 27.
32. Nikolaysen: Arch. Int. Med., 1920, xxv, 295.
33. Finzi: Virchows Arch., 1913, pp. 214, 413.
34. Friedman, G. A.: Jour. Med. Research, 1918, pp. 38, 449.
35. Mann: Jour. Exp. Med., 1916, xxiii, 203.
36. Kaufmann, J.: Am. Jour. Med. Sc., 1904, pp. 127, 646.
37. Crohn: Am. Jour. Med. Sc., 1918, clv, 801.

OBSERVATIONS UPON THE TREATMENT OF THE CHRONIC INTESTINAL INVALID.*

By John Bryant, M.D.,

Boston, Mass.

I. Introduction. The object of the present paper is to record some of the more definite impressions which have resulted from a ten-year intensive study of the chronic intestinal invalid. In 1910, when this study was first undertaken, information of value in regard

* An address delivered before the Hartford Medical Society, May 17, 1920.

to this particular type of patient was conspicuous by its absence. No one knew, and few seemed to care, what was going to happen to a class of invalids who, if seldom seriously ill, were practically always physically if not mentally inefficient. The present study has been prosecuted in the operating room, in various pathologic institutes of Europe, in medical libraries, and finally, for the past five years, by means of practical experience in the medical treatment of these patients. Various aspects of this study have been referred to in published articles.[1–15]

As a result of this work there has emerged from the haze of uncertainty a series of rather definite procedures, the application of which has resulted in the obtaining of a satisfactory percentage of improvement in the clinical condition of the type of patients under discussion and in their relative freedom from relapses. In a word the majority of the patients themselves have seemed satisfied with their new ability to carry on the daily affairs of life, and they have usually stated that this ability is in marked contrast to their previous years of physical and perhaps mental incapacity.

II. Mental and Physical Characteristics of the Patient. If the *genus homo* is subdivided into four species on the basis of visible physical development, under the headings of hypersthenic, sthenic or normal, hyposthenic and asthenic, we may discover by even a little investigation that the hyposthenic species today is not only conspicuous in point of numbers on a percentage basis, but that especially in the United States, the percentage of individuals belonging to this hyposthenic species is steadily on the increase. There are doubtless many reasons for this state of affairs. Three possible reasons follow:

1. The reduction of infant mortality.
2. The national dietary.
3. Labor-saving machinery.

Weakling infants, as a result of the crusade for reducing infant mortality, are being kept alive in an increasing ratio. If saved through the period of infancy these children are frequently fed during their growing stage (assuming that the feeding is adequate from a calory point of view) on diets deficient in minerals, especially calcium. Later, when adolescent or adult these individuals are often saved from or prevented from acquiring adequate physical development by the increasing use of labor-saving machinery in all our industries. The result of this sequence of events may be predicted as surely for the human as for the dog, or any other organism depending upon an adequate use of its musculature for the adequate muscular development upon which its well-being depends.

The adult hyposthenic may present symptoms predominantly nervous, circulatory, orthopedic or gastro-intestinal. Obviously, any combination of these groups of symptoms may also appear.

It is the gastro-intestinal variety of the hyposthenic species of the

genus homo, with which the present paper is concerned, under the title of the Chronic Intestinal Invalid.

The chronic intestinal invalid usually comes to the physician complaining of digestive symptoms and general poor health. When the complaints of such a patient are examined in detail, however, it will be found that many of them are almost identical with those presented by the other varieties of the hyposthenic species, especially the so-called neurasthenic variety. In general the chronic intestinal invalid shares with the other varieties of the hyposthenic species two distinctions, if they may be called such. On the one hand a careful routine physical examination is usually reported substantially negative, except that the patient is in a state of general poor nutrition and more or less obvious fatigue. On the other hand, although well-marked pathology is lacking, the patient feels, often looks and usually acts sick. Furthermore, such a patient will most persistently continue to say that he is sick, and inefficient both mentally and physically, no matter how often he is assured by well-meaning physicians that there is practically nothing the matter with him, and that if he will only cheer up he will be all right. In this case it is usually the patient who is correct and not the physician.

From the mental point of view the most characteristic finding is a constant overreaction to stimuli of all kinds. Such patients are consequently in a state of perpetual mental unrest. This is reflected in their changeability, the impossibility of their doing prolonged concentrated mental work, and their customary difficulty in getting adequate restful sleep at night. This fundamental excessive irritability is also suggested by a poor or capricious appetite, vasomotor instability, frequent floods of tears, apprehension and suspicion. Nervous energy is being wasted at a terrific rate in all directions, with the unavoidable result that sooner or later physical rest is enforced by collapse. This may proceed to a state in which nausea and vomiting are almost constant. An excessive flushing of the face on the slightest provocation contrasts markedly with the pallor observed in repose. A false vivacity, a peculiar harsh tension of the voice, excessive nervousness, tachycardia, precordial pain, cold and moist extremities and excessive sweating from the axillæ singly or in combination often accompany a spastic constipation and a muddy skin. Yet a fictitious cheerfulness on the part of the patient does much to mask continual bodily discomfort and emotional hypersensitiveness and to throw the casual observer off the track in regard to the true state of affairs.

Physically the bones are usually long and slender and the musculature is nearly always deficient. On account of the absence of a normal amount of erector spinæ muscle the vertebral spines, instead of being inconspicuous in a furrow between the heavy back muscles, are perhaps the most conspicuous feature presented to the observer on inspection of the patient's back. Intimately connected with the

usual fatigue posture is the collapsed lower thorax, the greatly narrowed costal angle, and what might be called the "clam-belly" type of abdomen prominent below but not above the umbilicus.

On inspection the pupils are usually dilated. The respiration is rapid and usually of the upper thorax type. The skin is likely to be dry, often rough, and usually yellowish dirty brown in color. The subcutaneous tissue is lacking in fat, and being without elasticity, feels to light pressure like a wet rag as compared with the rubber sponge sensation obtained on light pressure of the skin of a normal person. The muscles themselves are small, and if they can be relaxed are of poor tone and as lacking in resilience as the subcutaneous tissue.

One of the most striking signs on examination, associated with the discolored and abnormal skin, is a marked dirty discoloration of the entire eye socket. This sign[15] is so constant in its appearance in this type of case as to enable one to say almost at a glance that its possessor has some definite chronic intestinal difficulty; from experience it may be further said in connection with this eye sign that it often accompanies ileal regurgitation and is in itself a definite indication for diet. When diet is properly applied this eye sign and the muddy skin tend simultaneously to disappear.

Unless there is some infection about the teeth, tonsils or sinuses the general physical examination is usually reported negative. But local examination of the abdomen discloses a characteristic distribution of gas. On percussion it will be obvious that the gas is either generalized throughout the entire abdomen or limited to one of two locations. The more common of these locations is the region of the cecum and ascending colon. The second point of election for finding gas is in the sigmoid loop. Not infrequently, on careful palpation, one obtains a gurgling sensation of gas in the cecal region, suggestive of ileal regurgitation. Occasionally one may obtain a striking contrast on palpation between the size of the dilated cecum and ascending colon, and the rope-like spastic descending colon.

Locally such a patient complains of the classic symptoms of pain, gas and constipation. This pain is usually intermittent and associated with gas in the cecum or about the flexures. In addition there is another characteristic type of pain met with in the epigastric region, which, although simulating the pain of ulcer, is apparently largely connected with the narrowing of the costal angle, since it is permanently relieved simultaneously with the widening of this angle.

Gas formation is perhaps the most disagreeable feature of the situation, and in these patients one has to deal not only with the actual gas formation within the intestine but with an often considerable degree of inability to get rid of extraneous air swallowed with the food. When the intestinal tract is unusually spastic it is not infrequent to find that the patient has great difficulty in relieving

himself of gas in the stomach; if possible, it is with explosive effect. The same phenomenon holds true with regard to relief from gas in the rectum. The result is that although the particular patient may be manufacturing no more gas than his healthy neighbor, he is in much more constant discomfort on account of his inability to free himself from what gas is present.

A second point worthy of mention in considering the question of discomfort from intestinal gas is that when the tone of the intestinal musculature is poor the intestine is more easily distended by gas than normally, so that instead of there being a tendency for gas to move along in one direction or the other it remains in one place to the greater discomfort of the patient. This is especially true when there is a dilated cecum and ascending colon in conjunction with a spastic descending colon.

Constipation is for these patients almost normal. It is of one of two types, spastic or atonic. Except in unusual circumstances it will respond to proper treatment, so that instead of having to depend upon large quantities of irritating laxatives a reasonable degree of freedom from cathartics may be brought about by the use of laxative foods.

III. Relation of Physician to Patient. The relation of the physician to his patient, when the patient is one of the chronic intestinal invalids under consideration, presents certain contrasts to the conditions prevailing in the practice of acute medicine or surgery. In the practice of acute medicine the physician is called upon to see a patient who is presumably acutely ill from a definite disease. Consequently, in his analysis, the physician studying the acutely ill patient is likely to ask himself questions in somewhat the following sequence:

1. Is the patient sick?
2. From what disease is he suffering?
3. What can be done for it?

The physician's focus therefore is primarily upon a clinical entity, perhaps upon a self-limited disease of fatal intensity, and it is unavoidable that the seriousness of the disease may for the time obscure the individuality of the patient who presents the disease.

In the case of the chronic intestinal invalid the focus of the physician must be much more that of the family practitioner. It must be upon an individual who is not well. The patient has probably passed through a diagnostic mill, but may have yielded up almost negative findings. In spite of this the patient continues to complain of mental and physical debility. If the physician is human he must desire to help his patient. In order to throw light upon the obscure problem presented, the intelligent physician must begin his inquiry in somewhat the reverse order from that employed by his confrère who is devoting himself to acute medicine. Thus it is necessary to determine, first of all, with what kind of an individual

one is dealing and how he will react mentally and physically to his environment. The question of disease in this study remains almost always secondary to the question of the individual who is presenting the disease.

A second contrast between acute and chronic medicine becomes obvious when one considers that in acute medicine one clear-cut disease is usually diagnosed. In chronic medicine, on the other hand, the diagnosis is almost never single or simple. There is always a multiplication and a complexity of complaints. Possibly no one of these milder complaints would singly be of consequence. But in conjunction these mild disabilities may come to reach a sufficiently formidable total to prostrate the hyposthenic patient.

The chronic intestinal invalid may temporarily look, comparatively speaking, so well that no one will believe him to be sick. As a result he may get very little sympathy. Since he is exceedingly sensitive to injury, such a patient gradually learns to avoid giving strangers a chance to injure his feelings by the utilization of a mask of cheerfulness. It is impossible for the physician to begin to understand such a patient and to begin to learn with what material he must eventually deal in planning his course of convalescence until he has penetrated this defensive mental mask with which the invalid protects his hypersensitive feelings. For the purpose of penetrating this mask and arriving at an understanding of what is going on behind the mask the principal factor is time. The tenacity with which the patient will continue to remain protected by his mask (then suddenly coming out into the open as a hermit crab leaves his shell) is often amazing. For this reason it has been found desirable, when possible, to devote all the time necessary to the penetration of the defensive mask before the close of the first session with such a patient if real progress is to be obtained. On the basis of experience it may be stated that the penetration of this mask requires in proportion to the grade of mentality of the individual under consideration, anywhere from fifteen minutes to two or three hours. The result obtained, however, more than justifies the effort involved, for once such a patient is convinced of the reality of the interest of the physician in his personality and in his troubles, secrets no longer exist. The physician becomes at once friend, comforter, confessor. The necessity for arriving at this point as rapidly as possible is obvious when one considers the multitude of small details in the daily life of the patient, encompassed in the word environment, which may act to speed up or retard progress toward health.

IV. Diagnosis. The diagnosis in these cases is always a complex of social, mental and medical factors. Thus although the principal complaint which brings the chronic intestinal invalid to the physician may be of a gastro-intestinal nature, one not infrequently may find that industrial fatigue has been a predisposing factor in producing malfunction of the digestive system. In such a case relief of the

gastro-intestinal condition may be impossible without readjustment of the hours of work and the hours of rest. It is always a case of Mohammed and the mountain. But usually it is possible to readjust the patient or the work, or both, in such a manner that slow but continuous progress toward health is realized. There is no doubt that, if possible, it is often more desirable to perform such an adjustment than to remove the patient from all work, the mental effect of this removal being bad both upon the patient and his family if, as usual, there is a family.

The importance of considering the mental factor in arriving at a diagnosis has been referred to in a recent paper.[12] It is indicated also in an interesting recent article by Patrick.[21]

A third predisposing class of factors of very considerable importance in the production of gastro-intestinal disorders are the concomitant but not infrequently neglected medical abnormalities such as those recently reviewed by Bastedo.[16] It is, for example, not at all uncommon to find that mild orthopedic factors have been overlooked on account of the importance attributed by the patient to his gastro-intestinal symptoms. With women in the industries it is surprisingly common to find mild or even more serious degrees of abnormality of the generative functions as a background for digestive complaints. Thus, in one recent case, a telephone operator, aged twenty-five years, was referred for marked digestive troubles. She felt that her digestive troubles caused her nervousness and had convinced her previous physician to this effect. On careful inquiry it appeared that this girl had for years suffered from a very considerable degree of dysmenorrhea for about three weeks out of every four. She had previously mentioned this casually but had dismissed the matter as something that could not be avoided. It was possible, in the course of two or three months, to produce a very great improvement with regard to this dysmenorrhea so that pain only incapacitated her for two or three days. Parallel with this improvement came a marked improvement in the digestive conditions, and when last heard from the patient was back at work on full time.*

For the reason that apparently irrelevant details may prove of such importance as factors in treatment it is essential to devote unlimited time to the taking of a most complete history. It is perhaps not too much to say that with the majority of gastro-intestinal invalids an adequate history and a careful inspection of the patient may suffice to enable one to outline a reasonably successful plan of treatment, a treatment which in a considerable percentage of cases may lead to improvement in the patient's condition sufficiently marked to approximate cure.

* One year after beginning treatment, patient had just reported herself as cured. She has no longer constipation or digestive irregularity, and is for the first time in her life absolutely free from dysmenorrhea.

In general one may state, without danger of contradiction, that careful search will locate the primary etiology of very many cases of chronic intestinal disability in some focus outside the gastro-intestinal tract. This statement is but an amplification of the well-known remark that the stomach acts as a flag station for trouble in other portions of the gastro-intestinal tract far more often than it is itself primarily involved by pathology. Such etiologic foci will be found on search, in some of the other systems of the body, or in purely environmental conditions, reacting upon the patient through his impressionable mentality. A familiar example of this statement is the fact that in the laboratory one may cause a delay of almost an hour in the emptying of the stomach of a cat merely by allowing a dog to bark once or twice in the room in which the cat is being examined. It is thus evident that although the actual distress caused the cat by the dog was very temporary, the gastro-intestinal tract of the cat did not resume its normal function for a considerable length of time after the cause of the mental commotion had been removed.

V. TREATMENT. Rational treatment for the adult chronic intestinal invalid begins with preventive medicine in the child and in the adolescent intestinal invalid, since in probably 90 per cent. of all cases the defective gastro-intestinal tract and the unstable nervous system are conditions inherited rather than acquired. Unfortunately insufficient attention thus far has been paid to these patients during their developmental stages of growth, with the result that all cities and all hospital clinics provide for consideration large numbers of adult chronic intestinal invalids.

The active treatment of the adult chronic intestinal invalid divides itself into the early, intermediate and late phases of convalescence. There is, however, one underlying objective which must never be forgotten. This objective is the increased resistance of the patient to fatigue, and this increase in resistance to fatigue applies equally to the bodily and to the mental spheres. It is frequently necessary to build up from almost nothing the locomotor apparatus of the patient so that it will resist the ordinary strains of life. Simultaneously one must reduce, by educational and reëducational procedures, the overreaction of the nervous system to all forms of incoming stimuli.

During the early phase of convalescence it is frequently necessary to prescribe both internal and external rest. This period of complete rest is, however, usually of exceedingly short duration, since it is found that most patients do better at home rather than in a hospital, and with a definite if regulated degree of mental occupation and physical exercise.

The intermediate phase of convalescence is perhaps the most important. During this period, extending in time over one or two months, there must be an exceedingly careful gradation of physical

effort, so adjusted in length of time and so broken by frequent brief rest periods that in spite of the strains to which the patient is being put, one may obtain slow but gradual improvement in the condition of the general bodily musculature. During this intermediate phase there also comes a transition in the dietary from a somewhat limited soft and bland diet to one containing a larger variety of foods. One may also then introduce into the dietary the coarser foods which, if used earlier in convalescence, frequently result disastrously. In practice it has been found desirable to see ambulant patients twice weekly until the close of the intermediate stage of convalescence. A total of some twenty to thirty hours has usually been expended in personal attention to the individual chronic intestinal invalid by the time the intermediate phase is drawing to a close, and before such a patient begins, so to speak, to be able to navigate alone.

What is referred to as the late phase of convalescence is the period of time extending from the second or third to perhaps the eighth or tenth month after the patient is first seen, and from then on for perhaps two or three years. This is really a prolonged experimental phase during which the patient is enabled to find out, under occasional control, the precise extent to which he may, during his future life approximate what is called a normal standard of daily work with some prospect of being able to withstand it permanently, free from the specter of ultimate prostration. It is obvious that even the strongest individual may be broken by a sufficient amount of work. The object under consideration is, however, to determine how nearly normal an amount of work, a somewhat subnormal individual can accomplish without breaking. Once the high limit has been reached such an individual must realize that except for brief periods, under exceptional provocation, he can only exceed his limit under penalty of a definite danger of producing a recurrence of his symptoms. It is possible, however, during the progress of convalescence, to teach the patient methods by which, should he be forced to excessive efforts by family or other unavoidable calamities, he can, in the majority of cases, as soon as the excessive strain is over, work himself back without technical aid to a reasonably normal condition.

There are five distinct factors of fundamental importance in treatment; they are usually utilized in the following sequence:

1. Social.
2. Mental.
3. Dietary.
4. Orthopedic.
5. Glandular.

If one desires proof of the individual efficiency of these five independent factors they may be employed scientifically in consecutive sequence, so that in three or four weeks all five factors are being

simultaneously employed. It will be noted that of five factors fundamentally important to successful treatment only one applies directly to the digestive tract, 80 per cent. of all treatment utilized being therefore directed to objectives outside the gastro-intestinal system of the chronic intestinal invalid.

The necessity for considering the social status of the patient, not only with relation to character and hours of work but also with regard to the thousand and one other details which make up his daily life, is so obvious as scarcely to require mention except for the fact that it seems often overlooked. But frequently the first stage in relieving a patient of digestive symptoms may be the regulating of his hours of work, and a statement of the maximum length of time allowable for work, between rest intervals which must at first be passed in so far as possible in an absolutely prone position. Not less frequently nothing can be gained without modifying family friction or financial distress.

The mental factor has been referred to.[12] The methods of attack may be variable, but the result to be obtained is clearly a decrease in the overreaction of the patient to incoming stimuli of all kinds. One method used as a routine in the development of neuromuscular control is a system of very slow exercise,[10 13] which often acts as a kindergarten course in mental reëducation for the patient.

The dietary employed is based in part upon a consideration of the large amount of work by reputable investigators, which tends to prove the ease with which the intestinal flora can be changed by a modification of diet; also, upon a consideration of the fact that ileal regurgitation is an exceedingly common finding in the chronic intestinal type of invalid. Ileal regurgitation was, for instance, demonstrated in 80 per cent. of a consecutive series of 50 chronic intestinal invalids.[15] Eggs, meat and fish, as being potentially putrefactive, are at first absolutely excluded from the dietary, and the use of milk is restricted to the amount ordinarily employed in cooking. After a few weeks of complete restriction of the above foods it is very common to find that the patient's skin is distinctly less muddy. Slowly the yellowish color of the skin is replaced by white and then by pink, a transition which is greatly appreciated by the average woman patient. During this period of marked restriction of the diet, bran and the coarse vegetables are eliminated. No diet list is given, the patients being thus required to use their own brains in the working out of a suitable dietary. One advantage of this system is that the patient gradually acquires an adequate dietary for which he has the least possible dislike. If the dietary actually employed by the patient is written out and continually checked up at successive visits the results seem better from the point of view both of interest of the patient and of the physician than if a diet slip is handed the patient at the first visit. Eggs, meat and fish are rigidly excluded from the diet for at least one month. During the

latter part of this month, however, there is an increasing use of egg as a flavoring, in puddings or other cooked dishes in which the egg is finely divided by mixture with starches or the various vegetables. Meat gravies as relishes precede the use of meats as such. During the month of restricted diet liberal use is made of two special articles of food in conjunction with the usual fruits, starches, vegetables and fats. These two articles are cream cheese (or perhaps the ordinary cheese when used as a flavoring in various cooked dishes) and gelatin. The frequent use of flavored gelatins in the form of salads or desserts is encouraged. The necessary minerals, and the water and fat soluble vitamines, are provided for by the use of raw fruit and green vegetables and a good grade of butter. In this connection it is surprising to discover how few people are acquainted with the virtues both from a financial and an economic point of view, of chopped raw cabbage. This food as a salad with French dressing has been taken time and time again without the slightest discomfort or after-effects by patients who had previously stated that they could not possibly eat such a coarse vegetable.

At the end of a month or six weeks, if the progress of the patient justifies it (as evidenced by decreased constipation, lessened irritability, lessened disturbance from gas, better appetite and sleep, better color of the skin and fewer headaches) meat is put back into the dietary at first once a week. The intervals between the days on which meat is used are thereafter shortened according to circumstances. But in this type of case it has been found most unusual, if meat, eggs or fish as such can be handled with comfort more frequently than two or three times a week. The intermittent use of eggs, meat and fish has another virtue in addition to its economy and its tendency to discourage the growth of undesirable intestinal flora. If the patient has only to wait over one or two days of restricted diet before being allowed a day of full diet there seems to be much less desire for large quantities of these potentially putrefactive foods, which are handled with difficulty certainly in all patients with demonstrated ileal regurgitation.

An orthopedic factor requiring treatment is almost always present in the chronic intestinal invalid. Development of the skeletal muscles, and especially of the muscles responsible for the maintenance of correct posture, is considered a part of the daily routine in treatment. Although it would seem obvious it appears often forgotten that if a patient is not endowed with more than average viscera these somewhat mediocre viscera are certain to function better when given maximum opportunity by proper posture and muscle support than when they are compressed, as in the ordinary fatigue posture presented by these patients when first seen. The slow type of exercise previously referred to has the double virtue of being useful both from the mental and the orthopedic points of view.

During recent years there has been a wave of interest in what has been called ductless glandular or hormone therapy. In this field of work, proof seems unusually difficult. One may, however, assume that where there is much smoke there is at least a little fire, and it is incredible that such a voluminous literature should have grown up in relation to glandular therapy unless there were some justification for it. The student of this newer branch of medicine will find much to interest him in its application to the chronic intestinal invalid. The justification for its use in the type of cases under consideration results from the fact that in numerous personal cases one factor after another has been added to the treatment, each additional factor employed resulting in additional gain in the general condition of the patient. Having exhausted every other available factor, and having arrived at a stationary point in progress, it has been possible in many instances to obtain still further progress by the use of glandular therapy. For example, over five years of observation justify the statement that from a clinical point of view results may often be obtained from suprarenal therapy which are not possible without its use. A vast literature exists concerning the suprarenal gland and its possible utilization as an active therapeutic agent. Acute suprarenal deficiencies are becoming more frequently recognized. Subacute or chronic suprarenal deficiencies certainly exist in intensity between the acute deficiencies on the one hand and Addison's disease on the other. It is with these intermediate stages of suprarenal deficiency that the physician is concerned in the treatment of the chronic intestinal invalid, and there is little room for doubt that success is more certain with than without the utilization of suprarenal therapy in these invalids suffering, among other things, from chronic exhaustion. For this purpose, a standard grain v whole gland suprarenal preparation has been utilized in the majority of cases showing chronic exhaustion, with or without the accompanying muddy skin previously referred to. Other glandular preparations are frequently employed. Perhaps most often thyroid in amounts from one-tenth to one-fourth grain is useful. In women ovarian preparations are certainly of value in selected cases.

From a strictly pharmacologic point of view the only drug extensively employed is atropin. This is used in a strength of grain $\frac{1}{200}$, repeated from once to four times daily, according to indications. The two indications for which it is employed are to decrease spastic constipation and to decrease general irritability. It has often been found that a small amount of atropin is in itself sufficient to produce the difference between wakefulness and restful sleep, possibly as a result of its nervous sedative action.

In practice, on completion of the history, physical examination and the routine roentgen examination of the gastro-intestinal tract of which fluoroscopic study of an opaque enema is an essential element, the social and mental factors receive first consideration in

the progress of treatment. As soon as these factors are, so to speak, stabilized the diet is taken under serious consideration. In conjunction with diet frequent use is made of mineral oil, agar, yeast and atropin and every attempt is made to take advantage of habit formation and the natural rectal reflexes. As soon as the diet has become satisfactory the application of orthopedic procedures follows, and finally comes the use of the glandular preparations when indicated. Thus by the end of the first four to six weeks all five of these totally independent factors are being simultaneously employed in the effort to bring about, as rapidly as possible, an improvement in the general condition of the patient. Belts are rarely used, since they tend to decrease the faith of the patient in his own ability to carry himself through his day's work. Only slight attention is paid to the question of weight, provided there is not a progressive loss in weight. Not infrequently one may find an apparently healthy person of almost incredible thinness. On the other hand excessive fat is no guarantee of health. Usually, however, the very thin patients will put on at least ten to fifteen pounds in the course of a few months without apparent effort if otherwise satisfactory progress is being made.

Most authorities agree that the treatment of the chronic intestinal invalid is non-surgical in at least 90 per cent. of all cases. Conversely, recovery seems often to vary inversely with the amount of surgery to which the patient has been exposed. It is, however, certain that no patient should be operated upon unless the indications are imperative, for at least six months after intelligent non-surgical treatment has been instituted. During these six months, even if operation is later proved necessary for specific reasons, such as gall-stones or other definite pathology, the patient can have been brought to a status in which operation can be faced with much less probability of a subsequent slump in health.

VI. Prognosis. The application of the procedures above described to a series of 54 chronic intestinal invalids seen in an out-patient clinic, and reported[11] two years ago, produced the following results:

No improvement	7 per cent.
Improved	27 "
Improved plus	66 "
Total improved	93 "

This gives a total of better than 90 per cent. of definite improvement, although the condition of 27 per cent. of the cases marked "improved" left something to be desired.

In a consecutive series of fifty private patients, recently reported,[15] the following results were obtained:

No improvement	6 per cent.
Improved	8 "
Improved plus	86 "
Total improved	94 "

Compared with the out-patient cases it will be seen that although the total number of private cases considered as "improved" in all degrees was 94 per cent. as against 93 per cent. in the out-patient series, there is, on the other hand, a distinctly higher proportion of cases marked "improved plus" in the private patient series than in the out-patient series, the figure being 96 per cent. "improved plus" in the private as against 66 per cent. "improved plus" in the out-patient cases, or a difference in favor of the private patients of 20 per cent. considered as "improved plus."

It is therefore justifiable to tell the chronic intestinal invalid that he has a better than 90 per cent. prospect of improvement and that he has a better than 80 per cent. prospect of being very much improved as a result of a few months of non-surgical treatment. This is in itself a helpful point of view for the patient to have. The patient can also be told that he will, if careful, continue to improve for from one to three years after the completion of active treatment.

On the other hand it is misleading to speak of cure. Cure may be apparent but it is always conceivable that a sufficiently difficult combination of circumstances will arise to throw the bodily or mental mechanism out of gear. The trained patient will, however, be able rapidly to readjust himself with a minimum of medical assistance. The best advice to these patients is, after Oliver Wendell Holmes, to the effect that the surest approach to a happy old age is through taking care of an incurable disease.

VII. SUMMARY. 1. Certain impressions and observations resulting from a ten-year study of the chronic intestinal invalid have been presented.

2. Some of the mental and physical characteristics of the chronic intestinal invalid have been outlined.

3. Various contrasts in the practice of acute and chronic medicine, as applied, to the chronic intestinal invalid, have been indicated.

4. The importance of considering all possible factors outside of the gastro-intestinal tract in any attempt at adequate treatment of the chronic intestinal invalid, is referred to.

5. Five distinct and fundamental factors in treatment, all tending to increase the resistance of the patient to fatigue, have been considered.

6. The percentage of improvement obtainable as a result of applying the methods of treatment described, is stated on the basis of two different social groups of patients totalling 104 cases.

VIII. CONCLUSIONS. 1. Patience, persistence and a sympathetic understanding on the part of the physician are prerequisites for successful treatment of the chronic intestinal invalid.

2. The problem being complex and not simple, treatment must be applied from as many different angles as possible in order to produce maximum effect.

3. There are five distinct factors of fundamental importance in treatment. These are:

1. Social.
2. Mental.
3. Dietary.
4. Orthopedic.
5. Glandular.

The common objective of all these factors is increased resistance of the patient to fatigue.

4. These five fundamental factors in treatment must be applied in overlapping sequence in order to yield the maximum benefit.

5. The chronic intestinal invalid usually recovers at a rate inversely proportionate to the amount of surgery to which he has been exposed.

6. The physician who will take the time and trouble may promise the chronic intestinal invalid a 90 per cent. prospect of a reasonable degree of improvement, and an 80 per cent. prospect of a marked or satisfactory degree of improvement as a result of a few months of non-surgical treatment according to the methods above outlined.

7. Treatment which does not train the patient to avoid or to recover from future relapses with a minimum of medical assistance, falls short of what the chronic intestinal invalid has a right to expect from his physician.

REFERENCES.

1. Bryant: Internat. Abstr. of Surg., May, 1914, 449.
2. Bryant: Boston Med. and Surg. Jour., 1914, clxx, 795.
3. Bryant: Ibid., 1915, clxxii, 321.
4. Bryant: Ibid., 914.
5. Bryant: Ibid., clxxiii, 384.
6. Bryant: Ibid., 1916, clxxiv, 412.
7. Bryant: Ibid., clxxv, 237.
8. Bryant: Ibid., 572.
9. Bryant: Ibid., 649.
10. Bryant: Tr. Am. Gastro-enterol. Assn., 1918, p. 194.
11. Bryant: Ibid., 203.
12. Bryant: Ibid., 1919, p. 248.
13. Bryant: Am. Jour. Electrotherap. and Radiol., 1920, xxxvii, 85.
14. Bryant: Boston Med. and Surg. Jour., 1920, clxxxii, 629.
15. Bryant: Am. Jour. Med. Sc., December, 1920, clx.
16. Bastedo: Jour. Am. Med. Assn., 1920, lxxiv, 240.
17. Brown: Boston Med. and Surg. Jour., 1920, clxxxii, 187.
18. Herta: Wien. Med. Wchnschr., 1897, xlvii, 1651 and 1701.
19. Mayo: Jour. Am. Med. Assn., 1920, lxxiv, 376.
20. Palmer: Am. Jour. Med. Sc., 1914, cxlviii, 856.
21. Patrick: Jour. Am. Med. Assn., 1920, lxxiv, 69.

ON THE ETIOLOGY OF TYPHUS FEVER.*

By Edwin W. Schultz, M.D.,
STANFORD UNIVERSITY, CALIFORNIA.

For more than fifty years scientists have sought for the etiologic agent in typhus fever and still the cause remains undiscovered. During the past thirty years there have been more than twenty organisms held forth by various workers as the cause, or probable cause, of typhus fever. It is not my purpose to review the enormous literature which has accumulated from the earlier studies, interesting as that might prove to be; however, in view of the fact that the Great War somewhat interfered with the American profession keeping abreast with the contributions made along these lines in Europe, especially in Germany, it seems worth while to present the more important contributions which grew out of the serious typhus situation in Eastern Europe and, what seems to be, the real status of our knowledge at the present time regarding the causative agent of this disease.

To some the discovery made by Plotz[24] in 1914, and subsequently enlarged by him and his associates, [1 23 25 26 27] seemed to be the final solution of this difficult problem. Indeed, there are authors of text-books in bacteriology who have practically accepted this organism as the cause of typhus fever. True, the organism seemed to have more in its favor than did even the most promising of those previously upheld as the cause of typhus fever, but it cannot be said that sufficient evidence has been adduced to justify its being named "B. typhi-exanthematici."

The organism which Plotz described is a small pleomorphic, Gram-positive bacillus, which is non-motile, not encapsulated and not acid-fast. It is an obligate anaërobe and requires a rather select culture medium. Its length is said to vary from 0.9 to 1.93 microns, its breadth from one-fifth to three-fifths its length. The organisms are straight; occasional ones are slightly curved. The ends are rounded or slightly pointed. Coccoid forms are said to occur. With special stains an occasional organism shows a small polar body at one end; more rarely at both ends. The colonies usually appear in the culture tubes in about ten days; occasionally as early as the fifth day or as late as the nineteenth day. They appear first as opaque spots, which by direct light appear white. Subsequently they assume a "Y"-shaped growth, surrounded with a zone of brownish precipitate. The organism has been isolated from both Brill's disease, the mild American form of typhus fever, and epidemic

* From my "Closing Report of the Bureau of Medical Research" A. R. C. Commission to Poland, dated June 30, 1919, published by permission of the American Red Cross.

typhus fever. It has been grown from typhus infected animals and from infected lice. The organism shortly after isolation is slightly pathogenic for guinea-pigs; it loses its pathogenicity very rapidly. In the human host it induces the formation of specific agglutinins, precipitins, opsonins and complement-fixing antibodies. These are, however, detectable chiefly during the convalescent period. The agglutination readings average in the neighborhood of 1 to 200; only in one instance recorded going as high as 1 to 1600. These shall be discussed more fully further on.

In spite of the elaborate studies made by Plotz and his associates, their results cannot be said to show more than the fact that the organism is found in typhus fever patients. This much we must acknowledge in face of the cultural results and the serologic studies. But simply because an organism is found in a given disease does not license one to claim for it an etiologic role in the disease. The fact that it possesses a degree of pathogenicity for animals susceptible to the disease in question is of little significance unless the typical disease picture is reproduced. This includes not only the typical course of the disease but also the reaction induced by the disease, in other words, immunity relationships, if any occur. It is a well-known fact that typhus fever leaves an absolute immunity to further attacks in both man and animals. This immunity can be easily proved in animals by reinoculating them with the blood of a typhus fever patient subsequent to the animal's recovery from the disease, and in studying an organism isolated in typhus fever this procedure should be carried out extensively to determine whether or not it, in addition to producing the characteristic disease in a typhus susceptible animal (preferably a guinea-pig), also conveys definite immunity against subsequent inoculation with virulent typhus blood. Plotz and his associates did not succeed in reproducing even the disease picture in animals. The reason for this is laid to the extremely rapid loss of virulence of their organism on artificial media. But the fact remains that neither the disease picture nor what is more important, immunity reaction, was produced by inoculating their organisms into experimental animals. Their claim that the organism is the cause of the disease then rests solely upon cultural and serologic grounds and is unsupported by conclusive immunologic results.

In the autumn of 1915, Weil and Felix[46] isolated from the urine of typhus fever patients two strains of Proteus vulgaris which they named X1 and X2. These they found were markedly agglutinated by the sera from typhus fever patients, and on making control examinations learned that they were not dealing with ordinary saprophytes. The application of this discovery to the laboratory diagnosis of typhus fever was soon recognized by them. In the spring of 1916 they isolated another strain of this bacillus, also from the urine of a typhus fever patient, which they named X19.

This strain differed from the other two in that sera from typhus fever patients agglutinated the organism in dilutions many times higher than either of the other two—at that time one instance as high as 1 to 50,000. This organism has therefore, superseded the other two in the new serodiagnosis of typhus fever. It is not within the scope of this paper to discuss the technic of this method. In general it is not unlike the Gruber-Widal reaction. The reliability and diagnostic facility of this reaction has been confirmed by many workers and it has found a place in the diagnosis of typhus fever throughout Europe. It is diagnostic in practically 100 per cent. of the cases. The organism (Proteus X19) can be grown easily on ordinary nutrient media and may be kept for months without transplanting. In 1916 Dienes,[3 4] succeeded in isolating these X-strains from the blood of the typhus fever patients in 30 per cent. of cases which he examined. The reason why Proteus X19 has not been isolated in a higher percentage of cases was found by Felix[7] in 1917 to be due to the sensitiveness of the X-strain to the acid production of other bacteria in the urine and stools; to its sensitiveness to changes in media and, in the blood stream, to the rapid setting in of the bactericidal substances. Friedberger,[8] in 1917, on the basis of pathogenicity for guinea-pigs, agglutinins, precipitins, complement-fixation and Pfeiffer's phenomenon, maintained that Proteus X19 was probably the etiological agent in typhus fever. But in 1918 Landsteiner and Hausmann,[14] as well as Doerr and Pick,[5] and in 1919 Mollers and Wolff,[16] proved that Proteus X19 would not immunize guinea-pigs against typhus fever; that is, animals inoculated with blood from typhus fever patients subsequent to their recovery from Proteus X19 infection, developed typhus fever. We have here then an organism which, though occurring with remarkable regularity in typhus fever, apparently bears no etiologic relationship to the disease. This is especially interesting in view of the very pronounced serologic responses which the organism induces and the promptness with which the antibodies put in their appearance, generally within the first week of illness.

Now, let us compare the serologic responses induced by the Plotz bacillus with those produced by Proteus X19. It was previously stated that Plotz and his associates were unable to supply proof on immunologic grounds that their organism really was the cause of typhus fever and that the arguments for naming the organism "B. typhi-exanthematici" rest chiefly on a cultural and serologic foundation. The inadequacy of these arguments become obvious in a comparison of the agglutination readings of the two organisms in question. The average readings with the Plotz organism are figured from the readings given in one of Plotz's publications[25] and the average readings with Proteus X19 are obtained from one hundred readings made by Professor Oettinger[22] in studying the Weil-Felix reaction and the biology of Proteus X19. My figures show that

during the febrile period the Plotz organism is agglutinated by the patient's sera in dilutions of 1 to 8, at the time of crisis 1 to 113 and fifteen days after the crisis 1 to 220. The readings during the febrile period were for the most part negatives (readings below 1 to 50 were counted negatives), the highest reading being only 1 to 100. At the time of crisis they ran about half negatives, the highest reading being 1 to 800, and after the crisis they ran from negatives to 1 to 1400. Let us compare with these figures the averages of one hundred readings made by Oettinger in his studies on the Weil-Felix reaction. It will be observed that the agglutinins for X19 are far more concentrated and appear earlier in the disease. On the average eighth day of illness the agglutination readings average 1 to 2424, varying from 1 to 25 to 1 to 60,000 during the febrile period. On the average tenth day after the crisis the readings average 1 to 2540, one instance as high as 1 to 25,000 on the eleventh day. My own observation with the Weil-Felix reaction made while I was serving as bacteriologist for the American Red Cross Commission to Germany, satisfy me that the readings run a very high average, and in occasional cases exceptionally high. Indeed, a few of the workers have placed 1 to 200 as the lowest positive reading, which is practically as high as the average readings obtained with the Plotz organism at the time of crisis. It should be noted that the Plotz organisms show a degree of spontaneous agglutination which should also be allowed for in making this comparison. In short, we see that the agglutination readings obtained in using the Plotz bacillus are *nil* compared with those obtained in using Proteus X19, an organism which for these very reasons Freidberger felt justified in championing as the cause of the disease. Without proof on immunologic grounds and with serologic values which are negligible, what argument is there really left for upholding the Plotz bacillus as the cause of the disease?

Significance has also been attached to vague results supposed to have been obtained by attempted prophylactic immunization of people against typhus fever with the Plotz organism. In the winter of 1915–1916, Plotz, Olitsky and Baehr[26] inoculated 8420 persons, members of hospital, sanitation and other units in Serbia, Bulgaria and Volhynia, with a vaccine prepared from their organism. Out of this number six developed typhus fever during the four months of the epidemic. In other words the immunity, if any was really conveyed, was, at any rate, not absolute or complete. It therefore does not yield an added argument in favor of the organism being the cause of the disease. They were unable to obtain statistics as to the prevalence of the disease in the regions where they vaccinated so that one is at loss to even speculate on what possible decrease in the incidence of the disease might have resulted from these vaccinations. But it would seem that six cases among 8420 persons in a period of four months is not a negligible incidence of the disease.

Another important factor with which we are unfamiliar is the degree to which the various organizations enforced other prophylactic measures and the employment of typhus immune persons for the more hazardous duties in the handling and care of typhus fever patients, such as those of cleaning up the patients in the admitting office, etc. In short the results of the above experiments do not seem to furnish any added argument in favor of the Plotz organism being the etiologic agent.

But the question may be asked: Is not the fact that the Plotz organism has been grown from infected lice an excellent argument in favor of its being the causal agent of typhus fever? To this the reply would seem to be a question: Whence comes Proteus X19? It seems to me not improbable that the human infection is derived from the louse, and it is not unlikely that a number of other secondary organisms are introduced by the louse. The diplobacillus of Rabinowitsch,[30] also markedly agglutinated by the patient's sera, is probably another member of such a group. In brief, there are excellent reasons for believing that in typhus fever we have as a regular thing a state of mixed infection and that the organisms associated with the active virus of the disease are most probably introduced by the louse. There may be a state of symbiosis. It is worthy of note, in this connection, that Widmann,[49] in 1915 cultured a small Gram-negative, anaërobic, bacillus from normal lice. It is possible that quite an array of bacteria might be cultivated from both normal and infected lice.

This brings us to one of the most fascinating chapters in the history of research on the etiology of typhus fever, namely, that dealing with the development of our knowledge of the so-called Rickettsia. These studies were begun by Ricketts and Wilder[32] about ten years ago, but not until recently was there an appreciable advance made in our knowledge concerning them. Ricketts and Wilder,[32] in 1910, while working on the etiology of typhus fever in Mexico, made a large number of smear preparations from the digestive tracts of infected lice which they stained by the Giemsa method. They found that these smears contained large numbers of characteristic bipolar staining organisms. The thing that disturbed the significance of their observations at the time was the occasional occurrence of the same sort of organisms in smears which they prepared from normal lice. The fact that they dealt with two closely related organisms, one found exclusively in infected lice, has come to our notice through more recent investigations to be discussed presently. The observations of Ricketts and Wilder were confirmed by Prowazek[28] in 1913; by Sergent, Foley and Vialatte[39] in 1914, and by others.

In 1915 da Rocha-Lima[33 34 35] prompted by the earlier observations made on smear preparations of infected and normal lice, determined to study the lice by histologic methods, hoping that

this might clear up the confusion regarding these bodies. This proved to be a fruitful idea. It revealed the fact that a state of intracellular parasitism existed in typhus infected lice, involving the epithelial cells of particularly the gastrium. The control examinations showed that such a condition never occurred in non-infected lice—lice obtained from a typhus-free region. The involved cells of the gastric mucosa are found to undergo striking alterations so that their identification is frequently possible under the low power of a microscope. Within the cells the parasites, when few in numbers, are found to lie together in a group sharply rounded off from the rest of the cytoplasm. This is the picture early after an invasion, but as time goes on and the parasite multiplies the cells become entirely filled with the parasitic bodies and eventually cause them to be ballooned-out into the lumen of the stomach, protruding from the mucosa like droplets of fluid. Miss Sikora[40] observed the same involvement in the cells of the salivary glands. The parasite itself, da Rocha-Lima informs us, impresses one as a very small bacterium—smaller than M. melitensis or M. prodigiosus, but under very high magnification it appears not round but ellipsoid or olive-formed. These ellipsoid bodies lie for the most part in pairs, end to end, connected by a less intensely stained intermediate and surrounding substance. These double forms have the appearance of dumb-bells. Single forms also occur; the products of a recent division, but these are in the minority. Da Rocha-Lima estimates the single as 0.3 x 0.4 of a micron in size and the double or mature forms as 0.3 x 0.9 of a micron. Their staining qualities are of special interest. They stain very feebly or not at all with the ordinary bacterial stains, such as carbol-fuchsin, carbol-thionin, methylene blue, etc. They stain best and most characteristically with Giemsa, taking this stain differently than do bacteria. With this method they stain a pale ruby-red, almost the same coloration as nuclei take with this stain; however, not so bright a red, but more like the coloration which one obtains by this method on spirochetes and the tails of spermatozoa. Bacteria with this method generally stain a dark-red or an outspoken blue. The organism cannot be stained by Gram's method. Though many special methods were employed, all endeavors to cultivate the organism have failed. Da Rocha-Lima also noted the occasional occurrence of similar bodies in normal lice, but observed that these, without exception, lie extracellularly in the lumen of the digestive tract. These, undoubtedly, were the source of confusion in Ricketts' time when lice were studied entirely by smear preparations. Those of interest in connection with typhus fever are the intracellular forms found exclusively in typhus infected lice. For these da Rocha-Lima proposed the name, "Rickettsia-Prowazeki," in honor of these two scientists who gave their lives in studying the etiology of typhus fever. Other—what seem to be—species of this new group of

organisms have since been described, and to these I shall refer at the close of this review on the Rickettsia.

Let us now take up the evolution of this phenomenon of intracellular parasitism in infected lice. Da Rocha-Lima showed experimentally that the louse is incapable of transmitting the virus of typhus fever until at least five days after the louse has fed on a typhus fever patient. In other words a definite period for development or evolution is required by the organism in the intermediate host. Now, what light does da Rocha-Lima's histologic studies throw upon this phenomenon? Namely this, that the cells do not show an involvement previous to the fourth day after the louse has been infected, while after that period of time the phenomenon is present with regularity. His method of studying the development of the virus in lice is deserving of mention. The experimental lice were kept in a cleverly designed cage of very finely meshed screening (several of these which were left by him in Warsaw, Poland, at the time the Germans were driven from that place, were later utilized in our own studies). The cages containing the lice were tied to a patient twice a day for one hour and the rest of the time were kept in a thermostat at 33° C. He found that lice kept at a temperature of 23° C. between the usual feedings did not develop the Rickettsia and, furthermore, that injections of emulsions of the viscera of such lice into guinea-pigs did not result in an infection. Da Rocha-Lima showed also that the infection of the female louse may be inherited by its offspring.

Da Rocha-Lima[33] was the first to successfully infect guinea-pigs with typhus fever by direct inoculation of the virus in the form of emulsions prepared from the organs of virulent lice. The animals thus inoculated, after having undergone the usual course of the disease, were found to be immune to subsequent inoculation with blood taken from typhus fever patients. He found that the infectivity of such emulsions from lice was in direct proportion to the numerical content of Rickettsia. In one instance da Rocha-Lima succeeded in carrying on the louse virus, in passage from guinea-pig to guinea-pig, for nearly one year, during this time passing it through twenty-three animals. Blood from the eleventh passage was injected into a monkey, Macaccus sinicus, which developed the typical disease after an incubation period of eight days.

More interesting still are da Rocha-Lima's[33] studies on prophylactic immunization, using guinea-pigs as his subjects and a vaccine prepared from virulent lice. The lice used for the preparation of the vaccine were fed on typhus fever patients and kept under conditions which would ensure the greatest development of the Rickettsia. Emulsions were then prepared from the visceræ of these lice and the virus was attenuated by aging it for a number of weeks. The vaccine so prepared was administered hypodermically. The best results, absolute immunity of the entire series of animals, were

obtained by making three inoculations within the space of one week with a vaccine allowed to age for three weeks; the first dose containing an emulsion of five lice, the second ten and the third twenty lice. The experiments were controlled with normal guinea-pigs; the entire group, vaccinated and controls, received the usual infecting dose of blood from typhus fever patients. The non-vaccinated pigs contracted the disease, while the vaccinated ones, with a negligible exception, failed to show any reaction whatever.

It has been stated that other—what seem to be—species of Rickettsia occur in Nature. Before taking these up, let us review the features which separate the Rickettsia prowazeki from the rest, biologically, if not otherwise: (1) The Rickettsia prowazeki have a specific intermediate host, namely, Pediculus vestimenti. That the human louse is essential for the development of the Rickettsia-prowazeki was demonstrated by the researches of Nöller.[19] He fed pig lice and human lice on typhus fever patients at the same time. The Rickettsia developed in the human but not in the pig lice. There is one slight exception to this specificity, for Toepfer[42 43] and Toepfer and Schussler[44] whose studies confirmed for the most part da Rocha-Lima's work, claim to have observed the development of the Rickettsia prowazeki also in the human head louse, P. capitis. The biologic difference between P. vestimenti and P. capitis must be so small, if any, that the development of the Rickettsia prowazeki in the head louse need not be looked upon as a deviation from the specificity of the intermediate host. (2) The Rickettsia prowazeki are intracellular parasites of the louse.

Now let us turn briefly to the organism which was the source of confusion to Ricketts and Wilder and others since then, namely, the one occasionally found in normal lice. Nicolle, Blanc and Conseil,[17] working in Tunis in 1914, found that 5 per cent. of lice examined (smear preparations) in a typhus free region contained Rickettsia-like bodies. Brumpt,[2] in 1918, found them in smear preparations in 73 per cent. of lice taken from seven healthy war prisoners. This matter was also studied by da Rocha-Lima histologically. He found that whenever these bodies were found to occur in normal lice they were distributed over the surface of the gastric mucosa and never were found to lie within the cells even though they are found to lie in a rather thick layer against the mucosa. He further observed that though this organism was very similar to the Rickettsia prowazeki it was thicker and plumper and stained with greater ease than the Rickettsia prowazeki, though still not so easily as did the ordinary bacteria. Da Rocha-Lima named these Rickettsia-like organisms in normal lice, Rickettsia pediculi.

The same kind of organisms have also been found to occur in lice taken off patients suffering from Wolhynian fever, a disease similar to or synonymous with trench fever. These have been studied

particularly by Toepfer,[41] Jungmann[10 12] and by da Rocha-Lima.[15] They have been observed in as high as 80 per cent. of lice removed from patients at delousing stations, and are found to also occur in the form of a layer upon the gastric mucosa, though here one occasionally does observe a slight degree of intracellular invasion. Jungmann has named this organism, Rickettsia wolhynica.

None of the three above-named Rickettsia have yielded to artificial cultivation. This might cast a possible doubt on their actually being organisms, were it not for the fact that one species of this new group of organisms has recently been cultivated. The discovery was quite accidental. Nöller,[20 21] in 1917, while cultivating the Crithidia melophagi, a flagellate occurring in the sheep louse, Melphagus ovinus, found growing together with the Crithidia in separate colonies, a microörganism which in every respect looked like the Rickettsia. He named the organism Rickettsia melophagi. The following year Jungmann[11] confirmed and elaborated the studies of Nöller. The organism grows easily on the surface of a "sheep-serum-grape-sugar-agar" at 28° C. The colonies appear in six to eight days as minute, punctiform, translucent, round colonies, which on microscopic examination prove to be pure cultures of Rickettsia. Jungmann also studied the sheep lice histologically and found these bodies overlying the gastric mucosa, rarely noting even a slight intracellular involvement. He found that the infection was a constant one and, in a cleverly conducted research, established the fact that the lice obtained the infection by hereditary transmission and not from the blood of the sheep upon which they fed. The organism possesses absolutely no pathogenicity for any animals.

From the review of these researches on the Rickettsia we gather that an entirely new group of organisms has been discovered, a group seemingly occupying a position closer to protozoa than to bacteria.

It is thought by some that the Rickettsia prowazeki and the Plotz organism probably are one and the same organism. It is rather difficult to see wherein the likeness lies, and if the original description given by Plotz had not been later qualified in a remarkable way, there would, of course, have been no dispute as to their dissimilarity. Shortly after da Rocha-Lima's first publication on the Rickettsia appeared, Olitsky, Denzer and Husk[23] published the results of their studies in Mexico, in which they reported that they had grown the Plotz organism from infected lice. In this paper we get, for the first time, the remarkable fact that the Plotz organism is not always Gram-positive. They state: "In some of our blood cultures, however, smears made directly from colonies showed only bacilli which were completely decolorized by Gram's method. In other cultures the predominating organisms were Gram-positive, with numerous Gram-negative bacilli scattered throughout the

field. In subsequent subcultures the bacilli always became Gram-positive." Then they refer to the publication by da Rocha-Lima[33] as confirming their results. They state, referring to their cultures from lice, "In recent studies by da Rocha-Lima, further corroboration of this fact is made; he finds that infective lice harbor an organism of similar morphology in enormous numbers, especially in the stomach walls, and, remarkable to state, these organisms are Gram-negative." Strange to state, da Rocha-Lima does not acknowledge any such similarity. In the first place the Rickettsia are, strictly speaking, neither Gram-positive nor Gram-negative; they simply will not stain by Gram's method, because, for one thing, they do not stain readily with the simple bacterial stains. Outside of the unusual phenomenon with reference to the Gram-stain, Plotz does not mention any special staining qualities for his organism, and it is to be implied that it has the qualities of ordinary bacteria in respect to the simple stains. Besides, there is little in common morphologically between the two organisms. All attempts to grow the Rickettsia prowazeki seem to have failed in spite of the suggestions which might have grown out of the methods employed by Plotz and his associates. Finally, the one species of Rickettsia, Rickettsia melophagi, which has been cultivated, proved to be an aërobe, and it is not improbable, therefore, that the Rickettsia prowazeki is also an aërobe, rather than an anaërobe, as is the Plotz bacillus. The staining qualities, the sort of development in the louse, and the hereditary transmission of infection in lice resemble the activities of protozoa more closely than those of bacteria.

So much for the Rickettsia as observed in typhus infected lice. Though the grounds are less secure, it is, nevertheless, interesting to note the instances where Rickettsia-like organisms have been observed in the blood and tissues of typhus fever patients and experimental animals. Ricketts and Wilder[32] observed them in Giemsa-stained blood smears of typhus fever patients and in fresh preparations. They described the organism as a short bacillus which at first sight appeared solidly stained, but on minute examination showed an unstained or faintly stained zone across the middle. The fresh preparations also showed a differentiation of the forms into two halves, separated by a line or narrow zone of substance of a different refractive character, the organism possessing, not motility, but more or less rapid vibration. In 1911 Nicolle observed such bodies in the neutrophilic leukocytes of typhus infected chimpanzees, and Consiel and Conor[18] and Givino and Girard[9] in the same year in the neutrophilic leukocytes of typhus fever patients (Reder[31]). In 1913 Prowazek[28] made the same observations. He states that they occurred as oval and diplo-forms, lying in vacuoles, generally at the periphery of the leukocytes, and, with the Giemsa stain, colored a carmine-red, and were distinguishable from the neutrophilic granulations of the leukocyte. Da Rocha-Lima[36] has also observed

in blood smears from typhus fever patients as well as in histologic sections and smears made from tissues of typhus cadavers, structures which, in size, form and coloration, appeared the same as the Rickettsia. He tried out a large number of different staining methods, but was only able to demonstrate them when using the Romanowsky-Giemsa method.

In close association with the observation just described are those of Dr. Ludwig Anigstein, of the Central Epidemiologic Institute, at Warsaw, Poland, and myself, working together under the American Red Cross Commission to Poland. It was planned, as a part of our work, to carry on extensive studies on the distribution of these Rickettsia-like organisms in the tissues of typhus guinea-pigs and monkeys, and, as far as possible, human cadavers. But this part of the work did not materialize for reasons beyond our control. We were forced to limit our studies to blood smears and fresh blood from typhus fever patients. Doctor Anigstein prepared something like one hundred and fifty blood smears, representing about fifty distinct samples of blood from different periods of the disease. These he stained by various methods, chiefly with Giemsa and Leischmann stains. While these preparations were very interesting from the standpoint of striking nuclear changes, which will be written about later, only rarely were there bodies observed in the leukocytes which answered to Prowazek's description. One frequently sees, what seem to be exceptional inclusions of minute bodies, but to determine their morphology with accuracy is generally out of the question. However, bodies corresponding to the Rickettsia in shape, size and coloration were occasionally found lying free in the blood plasm.

To us the most interesting observations were those that we made with a dark-field, using a special Zeiss lens giving a magnification of at least 2000×. We examined by this method over fifty specimens of blood obtained from nearly as many different typhus fever patients in different stages of the febrile period of the disease. Of these 90 per cent. showed dancing bodies which in morphology, refractility and size were the same as those we observed in dark-field preparations of infected lice, which were made for comparison and afterward stained to further establish the presence of Rickettsia. These bodies occurred as single or ellipsoid forms but chiefly as the double or dumb-bell forms. It is extremely difficult to identify the single forms but the double forms are quite characteristic. The double forms really have the appearance of dumb-bells, two oval bodies being held together in their long axes by a less refractile fluid-like substance lying intermediately and frequently seen to surround the oval bodies. They are readily distinguished from the microsomes, or so-called blood-dust, in that these are much more refractile, generally larger and differ somewhat in morphology. As to numbers it was found that on

examining a capillary film between the slide and cover-slip under the magnification described, their number varied anything from one to five per field. No studies to determine their relative incidence in various periods of the disease were undertaken. The specimens were obtained by vena- and finger-puncture and special care was taken in the preparation of the glassware used. For financial reasons the work of the American Red Cross had to be materially curtailed and our work came to a premature close so that more extensive studies were out of the question. Twenty-five specimens of normal blood examined by the same method and with equal care failed to show these Rickettsia-like bodies.

I should like to now present certain arguments in favor of the etiologic agent of typhus fever being a protozoön or an organism related to the protozoa rather than a bacterium. In the first place the studies by da Rocha-Lima and others show that the louse as an intermediate host is not very unlike the anopheles mosquito in the spread of malaria. The louse does not serve as an intermediate host in the same way that the flea does in transmitting the Pest bacillus, by carrying the organism in its digestive tract. The phenomenon of intracellular parasitism in typhus infected lice, involving even the cells of the salivary glands, preceded by a definite period of development during which time the louse is non-infective, are features that one immediately associates with protozoan organisms. To this may be added the actual necessity of an intermediate host in the spread of the disease and the specificity of the intermediate host. The possibility of hereditary infection among lice must also be considered. Clinically, the exanthema and the characteristically limited course of the disease seem to point to a protozoan cause. Likewise suggestive is the characteristic onset with chills. Finally the Wassermann reaction in typhus fever points to a protozoan-like cause of the disease. Jablons,[13] in 1914, showed that during the florid period of the disease typhus fever may give positive Wassermann complement-deviation in practically 90 per cent. of the cases.

Conclusions. 1. There is no conclusive evidence that the Bacillus typhi-exanthematici of Plotz is the cause of typhus fever.

2. Proteus X19 has more in favor of its being the cause of typhus fever than the Plotz bacillus, but on immunologic and other grounds it appears that both of these bacteria are secondary invaders.

3. There is evidently a state of more or less mixed infection in typhus fever.

4. There may be a state of symbiosis.

5. The Rickettsia prowazeki are probably the cause of typhus fever.

6. The Rickettsia seem to constitute a new group of micro-organisms, probably more closely related to the protozoa than to the bacteria.

REFERENCES.

1. Baehr and Plotz: Jour. Infect. Dis., 1917, xx, 201.
2. Brumpt: Bull. Soc. de Path. exot., 1918, No. 11, p. 249.
3. Dienes: Feldarztl. Blätter, No. 11.
4. Dienes: Deutsch. med. Wchnschr., 1917, No. 15, xliii, 461.
5. Doerr and Pick: Wien. klin. Wchnschr., 1918, No. 30, xxxi, 820.
6. Felix: Ibid., 1916, No. 28, xxix, 873.
7. Felix: München. med. Wchnschr., 1917, No. 39, vol. lxiv.
8. Freidberger: Deutsch. med. Wchnschr., 1917, Nos. 42, 43 and 44, vol. xliii.
9. Gavino and Girard: Pub. de inst. Bacteriol. Nacionale de Mexico, 1911.
10. Jungmann: Berl. klin. Wchnschr., 1916, No. 12, liii, 323.
11. Jungmann: Deutsch. med. Wchnschr., 1918, No. 49, xliv, 1346.
12. Jungmann and Kuczynski: Ibid., 1917, No. 12, p. 359.
13. Jablons: Jour. Med. Research, 1914, No. 144, vol. xxv.
14. Landsteiner and Hausmann: Med. Klin., 1918, No. 21, xiv, 515.
15. Munk and Rocha-Lima da: München. med. Wchnschr., 1917, No. 44, lxiv, 1357.
16. Mollers and Wolff: Deutsch. med. Wchnschr., 1919, No. 13, vol. xlv.
17. Nicolle, Blanc and Conseil: Arch. de l'Inst. Pasteur de Tunis, 1914, ix, 84.
18. Nicolle, Conor and Conseil: Ann. de l'Inst. Pasteur, 1911, vol. xxv.
19. Nöller: Berl. klin. Wchnschr., 1916, No. 28, liii, 778.
20. Nöller: Ibid., 1917, liv, 346.
21. Nöller: Arch. f. Schiffs. u. Tropen-Hyg., 1917, xxi, 53.
22. Oettinger: Centralbl. f. Bakteriol., 1918, No. 60, lxxxix, 304.
23. Olitsky, Denzer and Husk: Jour. Infect. Dis., 1916, xix, 811.
24. Plotz: Jour. Am. Med. Assn., 1914, lxii, 1556.
25. Plotz, Olitsky and Baehr: Jour. Infect. Dis., 1915, xvii, 1. (Contains complete Bibliography to 1915.)
26. Plotz, Olitsky and Baehr: Jour. Am. Med. Assn., 1916, lxvii, 1597.
27. Plotz, Olitsky and Baehr: Ibid., 1917, lxviii, 576.
28. Hegler and Prowazek: Berl. klin. Wchnschr., 1913, No. 44, l, 2035.
29. Prowazek: Ztschr. f. Hyg. u. Infectionskrankh., 1916, No. 3, vol. lxxxii.
30. Rabinowitsch: Arch. f. Hyg., 1909, No. 4, clxx, 331.
31. Reder: Das Fleckfieber, published by Franz Deuticke, Leipzig, 1918. (Contains complete Bibliography to 1918.)
32. Ricketts and Wilder: Jour. Am. Med. Assn., 1910, vol. liv.
33. Rocha-Lima da: Arch. f. Schiffs. u. Tropen-Hyg., 1916, No. 20, p. 17.
34. Rocha-Lima da: Berl. klin. Wchnschr., 1916, No. 21, liii, 567.
35. Rocha-Lima da: München. med. Wchnschr., 1916, No. 39, lxiii, 1381.
36. Rocha-Lima da: Ibid., 1917, No. 1, lxiv, p. 33.
37. Rocha-Lima da: Med. Klin., 1917, No. 43, xiii, 1147.
38. Rocha-Lima da: München. med. Wchnschr., 1918, No. 52, lxv, 1454.
39. Sergent, Foley and Vialatte: Compt. rend. Soc. de biol., 1914, p. 101.
40. Sikora: Arch. f. Schiffs. u. Tropen-Hyg., 1916, No. 20.
41. Toepfer: München. med. Wchnschr., 1916, No. 42, xliii, 1495.
42. Toepfer: Deutsch. med. Wchnschr., 1916, No. 41, xlii, 1251.
43. Toepfer: Ibid., xlix, 1517.
44. Toepfer and Schüssler: Ibid., No. 38, p. 1157.
45. Weil: Wien. klin. Wchnschr., 1917, No. 13, xxx, 393.
46. Weil and Felix: Ibid., 1916, Nos. 2 and 31, xxix, 33 and 927.
47. Weil and Felix: Ibid., 1917, No. 48, vol. xxx.
48. Weil and Felix: München. med. Wchnschr., 1918, No. 1, lxv, 17.
49. Widmann: Ibid., 1915, No. 39, lxii, 1336.

ACUTE EPIDEMIC ENCEPHALITIS.

By Charles H. Miner, M.D.,
and
Stanley L. Freeman, M.D.,
Wilkes-Barre, Pa.

Introduction.—Many comprehensive papers have been published upon the subject of acute epidemic encephalitis by such writers as Economo, Wilson, Bassoe, Tilney, Neal, Barker, Flexner, House and others, so that it is not necessary to do more in this paper than to give a brief symptomologic analysis of our 20 cases which we have had the opportunity to study.

Our first case was seen in February, 1919, the others during 1920, seen in private practice, in the wards of the city hospital, in consultation and as representative of the State Department of Health.

The clinical phenomena or symptoms of this disease are caused by an acute infiltrative inflammation of the central nervous system, especially about the optic thalamus, the floor of the fourth ventricle and in the white matter of the brain and cord.

Classification.—Several writers have classified their cases into different groups according to the predominant clinical picture or to the portion of the nervous system involved. MacNulty, Tilney and Sabatini have made these classifications, which are helpful in calling attention to its resemblance to other diseases, but after a study of our 20 cases we have found that if the disease is seen in its early stages and observed during its entire course in nearly every case all the typical symptoms can be demonstrated.

Prodromata.—As Flexner has pointed out the prodromal symptoms have not been clearly defined. This has been due to the fact that most of the cases reported have not been observed until late in the disease. We have been able to study 18 of the 20 cases during the first week of their illness.

The disease usually begins with symptoms that resemble and have frequently been mistaken for influenza. They were catarrhal manifestations of the mucous membranes, of the upper respiratory tract with malaise, headache, general pains, mild or very severe, and frequently nausea, vomiting and constipation.

In some cases (as in Cases 1, 3, 5 and 15) these prodromal symptoms precede the typical symptoms by more than a week, while in others (as in cases 2, 4, 7, 11, 12 and 20) the prodromal period lasted only three days.

We were unable to determine the period of incubation, as no 2 cases occurred in the same family and there was no history obtainable of contact with a previous case outside the family. In 2 cases

the onset was sudden, in one (Case 6) with marked restlessness and delirium and in another (Case 19) with pronounced lethargy.

FIG. 1.—Case III. Sixth week of disease. Patient markedly improved, still shows partial bilateral ptosis, of eyelids and mask-like face.

FIG. 2.—Case IV. Patient improving; sixth week of disease still showing mask-like expression, ptosis and partial wrist drop.

Headache in varying intensity was present in all our cases.

Vomiting was only recorded in 8 cases and never was severe or continuous.

Constipation occurred in 14 cases, and this was also moderate in degree.

Other prodromal symptoms were severe muscular pains in the neck, shoulders and extremities in 12 cases, tonsillitis in 3 cases and nose-bleed in 1 case.

FIG. 3.—Case XVI. Patient shows ptosis of lids; mask-like face; lethargy marked; taken second week of disease.

The Disease.—The average duration of the fever was seven days. It was frequently present at the onset, but in some cases not until

FIG. 4.—Case XVI. Same taken third week of disease; shows profound lethargy; mask; ptosis; and dropping of lower jaw.

later in the disease. In mild cases it varied between 99° and 101° or 102°, but in fulminating cases, or those with complications, it

read as high as 107°. The age of patients varied from nine to seventy-eight years. There were twelve males and eight females.

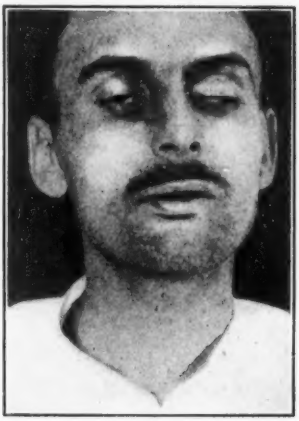


FIG. 5.—Case II. Fourth week of disease, showing bilateral ptosis; mask expression and left external squint.

Cranial Nerve Involvement.—Double vision was present in seventeen cases. We concur with William House that this symptom only

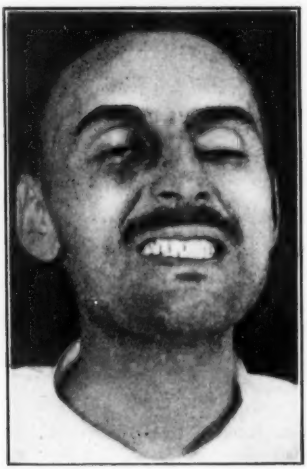


FIG. 6.—Case II. Fourth week, showing marked paralysis of both lids, particularly the left, and partial right facial paralysis.

lasts from two to four days in most cases, and was usually associated with some blurring of vision.

It was the first typical symptom of the disease to appear in 6 cases (Cases 2, 3, 4, 7, 12 and 13).

FIG. 7.—Case II. Second week of disease, showing marked catatonia of arms and partial wrist-drop.

This was clearly brought out in Case 2. A factory girl who used a large lever in her work, suddenly noticed that there were two levers instead of one and immediately reached out for the wrong one. She complained of this to the foreman of the factory.

FIG. 8.—Case II. Second week, showing catatonia of legs and general character of patient.

Third Nerve. This paralysis occurred in 18 cases. Bilateral ptosis was the most constant and striking cranial nerve symptom. It varied from a slight weakness to a marked paresis lasting throughout the course of the disease. The first definite improvement was often heralded by the raising of the eyelids voluntarily.

Fifth nerve paralysis was present in 9 cases. It was chiefly a

masseter muscle paralysis giving the symptoms of dropping of the lower jaw and difficulty in chewing.

Sixth Nerve. Six cases had an internal squint which was usually unilateral.

Seventh Nerve. Next in frequency to the third nerve involvement was that of the seventh nerve. The paralysis was either very slight or in some cases very pronounced. This was usually unilateral, involving particularly the right side, and when a bilateral paralysis occurred it was more marked on the right side.

The eighth nerve as far as we could tell by ordinary methods was not involved in any case.

FIG. 9.—Case II. Taken second week of the disease. Patient in deep lethargy. Note mask-like expression, marked ptosis of lids and dropping of lower jaw, due to weakness of masseter muscle.

The ninth nerve was affected, producing dysphagia in 7 cases.

Tachycardia was in evidence in 5 cases. Some claim this to be due to a tenth nerve involvement.

The eleventh nerve was affected in 3 cases involving the trapezius and sternocleidomastoid muscles.

A tremor of the tongue and slurring speech, such as that seen in general paresis, was observed in many cases, but no definite number can be given, however, as we failed to record this symptom in every case. This by some authors is conceeded to be a twelfth nerve involvement.

The most striking general symptom seen in our series of cases was a disturbance of consciousness, progressive in character, varying from apathy to coma. It usually developed by the end of the first week. In a few cases it occurred earlier and in others later in the course of the disease.

SYMPTOMATIC CHART OF CLINICAL SYMPTOMS.

| In order seen | Name | Age | Sex | Previous history of sylvenus | Character of onset | Prodromata | Headache | Vomiting | Constipation | Other symptoms prodromal | Duration of fever in days | Double vision | 3rd Nerve paralysis | 4th " | 5th " | 6th " | 7th " | 8th " | 9th " | 10th " | 11th " | 12th " | Stupor and lethargy | Delirium | Insomnia | Restlessness | Other paralysis | Ataxia | Catalepsia | Choreiform movements | Muscular fibrillation | Polyneuritis | Parkinson's mask | Eruption | Wrist drop | Toe drop | Asthenia | Kernig's sign | Babinski's sign | Reflexes, knee, Et. | Muscular atrophy | Incontinence of urine = feces | Spinal Fluid: Wassermann | Spinal Fluid: Character | Spinal Fluid: Pressure | Spinal Fluid: Cell count per C.M. | Spinal Fluid: Globulin content | Blood: Hemoglobin | Blood: Red cells | Blood: White cells | Blood: Differential count | Blood: Wassermann | Urine: Albumen | Urine: Sugar | Urine: Casts | Urine: Acetone or diacetic acid | Fever: Highest | Fever: Lowest | Date of disease when first seen | Duration of disease | Improved | Died | Complications | Sequelae |
|---|---|---

This lethargy is not as profound as one would expect from the appearance of the patient, as they were easily aroused when spoken to and answered questions intelligently in the early stage. As the lethargy increased it became much more difficult to elicit responses. Some cases, while apparently lethargic, were really restless and excited with muttering delirium. It was only during the early stage of lethargy that we noted catatonia as a symptom. The lethargic state lasted from two weeks to three months in our series, disappearing gradually.

Delirium was a symptom in 17 cases. It occurs usually early in the disease and of a mild type. In 2 cases it was maniacal in nature. The patients seem to realize their actions in mild cases. In a few restraint was required. Insomnia was present in 16 cases. Many cases required hypnotics.

Restlessness was evident in 13 cases. This restlessness existed in all forms, from a sense of general discomfort with inability to assume a comfortable position, to a marked tossing about or attempts to get out of bed.

Catatonia was an interesting and unusual symptom to be seen in an acute epidemic disease and was present in 16 cases. It has a distinct place in the course of the disease and occurs early during the period of lethargy. In no one case did it appear before the onset of lethargy, and as the lethargy tended to be prolonged the catatonia began to disappear. It could be elicited best by raising the arms or legs. They would remain in this position for some time and then tend to drop slowly to their normal position.

Ataxia was noted in 18 cases and occurred usually at the onset of the disease. It was most pronounced in the arms and was of an intentional type, noticed more particularly when the patient was asked to pull down his sleeve or reach out for some object. The ataxia of the legs was evident in many cases and resembled in some cases the cerebellar type, causing the patient to circle to the left or right.

Choreiform movements were in evidence in 11 cases. They resembled all the types seen in chorea from the mildest to the most severe, but particularly affecting the right side. Other writers have reported on this condition but not in nearly as large a percentage of cases. When the symptom is pronounced it must be differentiated from true chorea.

Muscular fibrillation, a marked twitching of various muscles or muscle groups, existed in all cases charted, or 100 per cent. It was a very interesting and suggestive symptom, and in fact so distinctive and characteristic as to make one immediately suspect encephalitis when it is seen. Most of these cases presented twitching (particularly of the lips, nasal muscles). Some had twitching of the arms and legs and a few of the intercostal and abdominal muscles. The rate of twitching was about 75 per minute, and in our opinion is a

most convincing symptom. It may be general or local or it may occur in all parts of the body at different intervals.

Parkinson's mask occurred in all but one case, and when once seen it cannot be forgotten, as it certainly resembles the mask seen in paralysis agitans and together with the muscular tremor has led many writers to describe a paralysis agitans group.

The tremor noted in 100 per cent. of the cases was coarse in type and increased by purpose—in other words, an intention tremor. This disappeared during actual sleep and returned upon awakening the patient.

Eruption was present in 3 cases, in 2 it was herpetic upon the face and legs and in 1 it was a marked purpura of both arms, legs and shoulders. This patient finally developed gangrene of the toes. The gangrenous area was on all toes and extended to the ankle.

Among the other paralyses seen in our series were 5 cases presenting paralysis of the arms and legs. It was noted that these all began on the right side. These cases resembled anterior poliomyelitis, but were associated with a severe polyneuritis. As the neuritis improved so did the paralysis.

Partial wrist-drop and foot-drop occurred in 4 cases and wrist-drop alone in 1 case. The polyneuritis was marked in these cases and the paralysis was usually bilateral. This can be seen in some of the photographs.

Euphoria, a sense of well-being, as described by House, was present in our cases, except in those cases associated with polyneuritis.

Asthenia was present in 100 per cent. of cases and differed in degree. It is one of the symptoms which characterizes the disease. It is with difficulty they can move about in bed, and in some cases they are absolutely powerless. This lasts for a considerable period after convalescence has been established.

Reflexes were exaggerated in 13 cases, normal in 4 cases and decreased in 3. They are not constant and varied with the stage of the disease. In the early stages almost all were increased. As the lethargy developed they gradually decreased and returned to normal late in the disease.

Kernig's sign was not constant either, although slightly positive in 9 cases. There were stages during the disease when Kernig's sign would be markedly positive, associated with muscular hypertonus and later when it would be absent, so that the conclusions drawn are that it is at first absent, increased during early lethargy and decreased as the case gets well.

Babinski's reflex was conspicuous by its absence, it was not present in any one single case and was looked for all through the course of the disease.

Muscular atrophy was only seen in those cases which developed polyneuritis or paralysis.

Incontinence of urine and feces were noted in 4 cases, and then only during deep lethargy.

Spinal fluid, it is interesting to note, was disturbed very little in our cases, although other writers, such as Barker, Strauss, etc., found an increased cell count and increased globulin content. We were able to make analysis in only 11 cases, this being due mainly to the fact that most of them were private cases, and great objection was made by their families to lumbar puncture. The analyses of the spinal fluids shows in each case perfectly clear fluid, no sediment on standing, no increase in globulin content, and came out usually under normal or slightly increased pressure. Spinal fluid Wassermann was negative in all and cell count averaged between seven cells per cubic millimeter, which was the lowest count, and thirty-six cells per cubic millimeter, the highest count.

Complete blood analyses were made in 9 cases. Varying degrees of anemia were noted, the lowest hemoglobin count being 40, the highest 96. Red cells ranged from 2,500,000 to 4,200,000. Blood Wassermann was negative. In all there was slight leukocytosis. 7900 to 14,600. Differential count showed polymorphonuclear increase ranging from 62 per cent. to 83 per cent.

Urine was negative except for a slight trace of albumin in 6 cases. Sugar, casts, acetone and diacetic acid were negative. Functional tests when done gave negative results.

Duration of the Disease.—It is impossible to state as yet the exact duration of this disease, as many of these cases are still running their course and are by no means well. The chart will give a fair idea of the length of time these cases run, for example: The shortest case was four days, ending in death at that time; the longest one hundred days, and still the disease is in evidence.

Prognosis.—Of the 20 cases 15 are improving, 1 is well, 1 is dangerously ill and 3 died. Death in these cases was due to respiratory failure. In 3 there were complications, namely:

Case 1. Marked gangrene. The most severe we have ever seen, of toes of both feet, probably trophic in nature. Also lobar pneumonia.

Case 6. Developed otitis media.

Case 19. Developed pneumonia.

In only 4 cases so far has a sequela been found (Case 1, a very marked nystagmus of both eyes, and in the other 3 cases paralysis of eye-lids and extremities).

Conclusions. We believe from our study of these cases that in any case presenting fever, cranial nerve paralysis, particularly the third and seventh nerves, accompanied by stupor or lethargy, with muscular fibrillation and tremor, together with mask-like face, a diagnosis of epidemic encephalitis should be seriously considered.

We have found the spinal fluid practically normal in all cases, but believe a spinal puncture should be made when possible to exclude

cerebrospinal and tuberculous meningitis, anterior poliomyelitis and cerebrospinal syphilis.

There are many other conditions that may be confused with this disease, yet we feel that cases of acute encephalitis, as we have seen them, are so characteristic and have so uniformly the same symptom-complex that the diagnosis can easily be made by one who has once seen the disease. Other writers speak of mild, ambulatory or abortive cases when there would be considerable difficulty in establishing a diagnosis, but we have not seen any of these cases. We wish to express our appreciation to our colleagues who so courteously and willingly coöperated with us in studying and following up these cases, namely, Dr. H. L. Whitney, of Plymouth; Dr. S. H. Rynkiewicz, Kingston; Dr. Vivian Edwards, Edwardsville; Dr. M. C. Rumbaugh, Dorranceton; Dr. J. W. Kirschner, Luzerne; Dr. John J. McHugh and Dr. R. S. Woehrle, Parsons; Dr. Richard J. Burke, Miners Mills, and Dr. Walter Davis, of Wilkes-Barre, Pa.

The photographs and lantern slides of these cases were carefully made by Dr. S. H. Rynkiewicz, who devoted much time and labor, often under great difficulty in order to secure these photographs.

Report of a severe case complicated by gangrene. (Brief notes.)

Patient, Mrs. R. H. W., married six years, one child, aged thirty-five years.

Patient was taken with a sudden high temperature of 103.5°; severe headache and painful sore-throat; culture of throat showed hemolytic streptococcus, short chain type; throat had false membrane over tonsils; pains in extremities, especially of legs and arms; fifth day—marked purpura; eruption over legs and arms, trunk, neck and face free. Patient refused to eat, nasal tube used for feeding; irritability of muscles of arms and legs; extremely tender over course of nerve trunk; muscular twitching of hands resembling trembling in paralysis agitans; marked flexion of wrists similar to wrist-drop. Patient restless; cries out; insomnia, delusions ptosis of eyelids. Patient became very drowsy, sleepy, lethargic, and could only be aroused by talking to in a loud voice; answers rational; said she felt better. There was a slight internal squint; partial paralysis of third nerve; partial paralysis of muscles of deligation; reflexes greatly exaggerated. No Babinski; no Kernig; marked polyneuritis of arms and legs. Patient lethargic until twentieth day, when temperature dropped; patient became brighter; hopes are entertained for recovery. Patient remained in this condition for four days when paralysis of muscles of the lower jaw became more severe; no rigidity of muscles; feet showed toe-drop. Twenty-eighth day patient developed paralysis of epiglottis and inspiration pneumonia; temperature rapidly soared to 107.8°, and on thirtieth day the patient died of the disease.

Purpura cleared up on twelfth day of the disease but was followed by a marked polyneuritis; this was followed by marked atrophic changes of lower extremities, causing blebs filled with serum over the dorsal of both feet together, with gangrene of all toes, which remained until the end.

Physical Examination. Shows mask-like appearance of face partial paralysis of both eyelids; dropping of jaw; paralysis of muscles of deligation. Reflexes exaggerated; marked flexion of wrist and foot; marked purpura of legs and arms, tenderness along the nerve trunks (polyneuritis). Right facial paralysis.

Report by Dr. George W. Carr of eye-grounds reveals no choked disk; no albuminuric retinitis. Eyes react to light and accommodation. Ear and mastoid region negative. Nose shows deflected septum. No Kernig; no Babinski; no clonus; marked irritability of muscles; delusions marked at times and at other times perfectly clear. Urine reports negative, except for slight amount of albumin. Blood analysis showed a marked secondary anemia, with slight leukocytosis. Widal and blood Wassermann negative. Spinal fluid showed no increased pressure, no cloudiness upon standing, perfectly clear, no increase in globulin, cell count 12 per cm.; spinal fluid Wassermann negative; blood and spinal fluid culture, negative.

Culture from the throat gave a hemolytic streptococcus.

Dr. George Morris Piersol, of Philadelphia, saw this case in consultation.

ACUTE EPIDEMIC ENCEPHALITIS (TWENTY CASES). MOST PROMINENT SYMPTOMS. AGE NINE TO SEVENTY-EIGHT YEARS. SEX: MALES, TWELVE; FEMALES, EIGHT.

Headache	100 per cent.
Lethargy	100 "
Muscular fibrillation	100 "
Asthenia	100 "
Cranial nerve paralysis	100 "
(3d nerve 90 per cent. = 7th N. 75 per cent. = 5th N.	45 "
Ataxia	90 "
Parkinson's mask	95 "
Delirium	85 "
Catatonia	80 "
Insomnia	80 "
Double vision	75 "
Restlessness	65 "
Reflexes increased	65 "
Choreiform movements	55 "
Polyneuritis	45 "
Kernig's sign	45 "
Paralysis of arms and legs	25 "
Average duration of fever	7 days
Eruption	15 per cent.
Mortality to date	15 "

RECURRENT TYPE I PNEUMONIA: SERUM TREATMENT OF TWO ATTACKS ONE MONTH APART:*

By Henry M. Thomas, Jr., M.D.,
BOSTON, MASS.

As an illustration of several important points in the immunology and therapy of lobar pneumonia the following case is reported: Opportunity for complete investigation of the condition was not afforded, but enough data are on hand to make an interesting study.

Our knowledge of immunity—active or passive—in lobar pneumonia is still in a comparatively indefinite state.[1]

1. Does one attack confer any immunity?
2. Are successive attacks more liable to be caused by a pneumococcus of a different type or of the same type?
3. Does prophylactic inoculation with killed cultures produce immunity?
4. Can passive immunity be produced by the injection of anti-pneumococcus horse serum?

The blood of patients recovering from lobar pneumonia was shown[2] to possess, at the time of crisis and shortly after, the power to protect laboratory animals from lethal doses of the type of pneumococcus which caused the pneumonia. Specific antibodies, agglutinins[3] and opsonins[4] have been similarly demonstrated, but their demonstration, in some cases, becomes impossible within a relatively short time after recovery. Skin tests using bacterial antigens[5] have been tried but are as yet unsatisfactory. Complement-fixation tests[6] have not added to our information and no one has shown the presence of true pneumotoxin and antitoxin.[7] These statements show quite clearly that we obtain no practical aid from laboratory methods in demonstrating more than a fleeting immunity to lobar pneumonia following recovery.

Available information as to immunity afforded by an attack is extremely limited. That people have repeated attacks of pneumonia is well known, but the opportunity for studying several attacks in one individual is rarely offered, so that the degree of active immunity produced by one attack is still undetermined. A case in the Rockefeller series[8] is known to have suffered from sixteen attacks of pneumonia, the last two attacks being studied in the Hospital of the Rockefeller Institute. The bacteriologic history begins with the twelfth attack (1916), which is reported to have been caused by Pneumococcus Type I. The next attack (1916) was caused by Pneumococcus Type III and the fourteenth attack (1916) by Pneumococcus Type IV. During the fifteenth (1916) and sixteenth

* From the Pneumonia Service, Boston City Hospital.

(1917) attacks Pneumococcus Type III was isolated. At the time of the last attack of pneumonia he also suffered from acute double otitis media, with cervical and submaxillary lymphadenitis. He was again admitted a year later (1918), suffering from chronic ethmoiditis, left; chronic sphenoiditis, left; acute otitis media, left; acute cervical adenitis, left. He received inoculations of heat-killed pneumococcus vaccine, including the three fixed types, in 1916, after his fifteenth attack and again at the time of his last admission. He has not had pneumonia since February, 1917.

This patient had five attacks of lobar pneumonia within a period of a little more than one year—three of these attacks were caused by the same organism, Pneumococcus Type III, which may have been harbored in an infected sinus. That he recovered from sixteen attacks of lobar pneumonia suggests some degree of immunity, but obviously not enough to prevent the attacks.

The only other patient observed in two attacks of pneumonia at that clinic[8] was a man who had a Pneumococcus Type I infection of the right lower lobe in March, 1918. He was treated with serum and recovered uneventfully. About one year later he returned with a typical right lower lobar pneumonia, again Pneumococcus Type I. He was desensitized, treated with serum and again recovered.

From February, 1919, when the pneumonia service was started at the Boston City Hospital, to May 1, 1920, there have been two cases other than the one reported in this paper, admitted twice with lobar pneumonia.

M. G., aged twenty-four years, admitted May, 1919; lobar pneumonia, Pneumococcus Type II; readmitted October, 1919; lobar pneumonia, Pneumococcus Type I.

F. P., aged seven years; admitted May, 1919; lobar pneumonia, Pneumococcus Type IV followed by pleural effusion; readmitted September, 1919, with lobar pneumonia, Pneumococcus Type II atypical.

No definite conclusions can be drawn from these four cases.

The efficacy of prophylactic inoculation, on the other hand, has been well demonstrated,[9] and from this fact we may infer that recovery from an attack leaves a certain immunity, the points in doubt being its degree and duration. An attack of typhoid fever usually produces complete and lasting immunity, whereas prophylactic inoculation must be repeated every few years. Arguing from analogy, an attack of lobar pneumonia should produce a much more satisfactory immunity than prophylactic inoculation, or, in other words, a very fair degree of immunity.

Blake and Cecil,[10] announcing the titles of their articles to appear in the coming numbers of the *Journal of Experimental Medicine*, speak of Paper V, "Active Immunity against Experimental Pneumococcus Pneumonia in Monkeys following Vaccination with Living Cultures of Pneumococcus," and Paper VI, "Active Immunity Following

Experimental Pneumococcus Pneumonia in Monkeys." They evidently have been able to demonstrate active immunity following an attack of lobar pneumonia in monkeys as well as after prophylactic vaccination. This agrees with the current opinions on the subject of immunity in lobar pneumonia in man, and it is, as far as we know, the nearest approach to an actual demonstration that has been brought forth.

Lastly, that Type I, lobar pneumonia, may be aborted and cured by intravenous administration of Antipneumococcus Type I horse serum[11] is proof of the production of passive immunity. How long does this passive immunity last? For an absolute answer to this question the substance producing the immunity should be known and tested for until its disappearance from the blood stream. (The question of local immunity need not be discussed at this time.) Agglutinins, precipitins, opsonins and bacteriotropins are shown to disappear rapidly, but the exact duration of their presence in the serum has not been carefully worked out. Whether the curative effect of anti-pneumococcus serum depends on one or all of these factors,[12] or even others yet undescribed, is still a matter of conjecture; therefore the duration of passive immunity for pneumonia must at present remain undetermined. If we turn to a condition in which passive immunity has been carefully studied, *i. e.*, diphtheria, we see that this immunity diminishes very rapidly, so that it cannot be demonstrated at the end of four weeks.[13] There is no evidence that passive immunity to pneumonia lasts any longer than this. We fully realize the unreliability of this comparison, however, as a toxin-antitoxin mechanism in pneumonia has never been conclusively shown.

Record of Case.

J. B. Aged twenty-nine years; married; colored; meat handler.

Admitted. November 29, 1919.

Complaint. Cough, pain in chest.

Family History. Unimportant; wife and one child living and well; no miscarriages.

Personal History. Measles, mumps, whooping-cough and chickenpox in childhood. Malaria nine years ago. Lobar pneumonia, left upper lobe (no bacteriology), April 19, 1918, in Boston City Hospital. Wassermann positive, April 30, 1918.

Nocturia. One to two times for past six months.

Venereal. Denied.

Habits. Coffee, two to three cups daily. Whisky, two to three drinks; beer, three or four drinks daily before prohibition. Tobacco, chews twenty cents worth a week.

Weight. Best 175 pounds, three months ago. Average, 165 pounds. Last weight, 166 pounds.

Present Illness. Sudden onset yesterday, November 28, 1919, with chill, pain in left side, severe malaise and bone aches. Cough with brown, sticky sputum. Last night vomited and developed "pleurisy pain" in the left chest.

Physical Examination. Well-developed and nourished colored man, complaining of severe pain on inspiration.

Lungs. Slight dulness below left clavicle. In this region and high in the left axilla breath sounds are bronchovesicular in quality, whispered and spoken voice sounds are increased and following cough there are persistent medium rales.

November 29. Wassermann strongly positive. Blood culture positive, Pneumococcus Type I. Sputum, mouse inoculation, Pneumococcus Type I. Skin test (horse serum), negative.

November 30. 11.30 A.M., 1 c.c. horse serum intramuscularly. 12.30 P.M., 100 c.c. antipneumococcus serum, Massachusetts State Board of Health Laboratory No. 50, given intravenously very slowly. 1.15 P.M., ten minutes after completion of serum treatment, patient developed a diffuse urticaria which was easily controlled by adrenalin, $\frac{1}{1000}$ solution ♏x followed in fifteen minutes by adrenalin $\frac{1}{1000}$ solution ♏vii.

December 1. Temperature normal; signs in chest slightly more marked than yesterday. White count, 20,200. Roentgen ray of chest: left diaphragm higher than right; left apex dense homogeneous shadow; pneumonia. Urine: albumin, slightest possible trace; sediment, few white blood cells.

December 2. Lungs clearing rapidly, temperature remains normal.

December 3. White count 5800.

December 4. Urine: albumin, 0; sediment, 0; Wassermann negative.

December 6. Lungs clear. Up and around ward. White count 7400.

December 8. Two nights ago patient complained of slight itching. There were a few urticarial wheals to be made out.

In other respects condition is absolutely normal. Patient insists on going home on account of illness of wife. To continue convalescence at home. Discharged cured.

Diagnosis: Lobar pneumonia, left upper lobe. Pneumococcus Type I.

From subsequent questioning it was learned that the patient remained quietly at home for several days, but felt so well and strong that about December 12 he returned to work in a meat market, which was damp and cold.

Second Admission. Admitted December 30, 1919 (thirty-one days after preceding admission).

Present Illness. Sudden chill while at work yesterday. December 29, slight headache and general malaise, cough with yellow sputum, which became reddish this morning. Vomited once.

Physical Examination. Over right upper lobe percussion note is dull; breath sounds are tubular; voice sounds tubular and nasal in quality. Few medium rales at left apex.

December 30. Sputum Pneumococcus Type I, Bacillus influenza. Blood culture, negative. Wassermann strongly positive.

December 31. White count 18,800.

12 M. Skin test (horse serum), very slightly positive (?). 1 P.M., 1 c.c. horse serum intramuscularly. 2 P.M., 100 c.c. Antipneumococcus Type I serum, Massachusetts State Board of Health Laboratory No. 51, administered intravenously, the first 30 c.c. given slowly over a period of thirty minutes and the remainder in fifteen minutes. No immediate reaction was noted during treatment, but twenty minutes later patient had a mild chill and complained of slight itching.

December 31. Roentgen-ray of chest; dense shadow localized in right axilla. Temperature fell during afternoon and night, reaching 99° rectal at 5 A.M. (January 1, 1920), but rose again to 103° rectal at 9 A.M.

January 1. 10 A.M. 100 c.c. Antipneumoccocus Type I serum (Laboratory No. 51) given intravenously; no immediate reaction; no chill.

January 2. Temperature, pulse and respiration fell gradually, reaching normal this morning. Patient looks and feels much better.

January 7. Lungs clear. Patient up one-half hour.

January 11. No signs of serum sickness, condition excellent.

January 11. Patient insists on going home. Has not had any evidence of serum sickness. Discharged cured.

Diagnosis: Lobar pneumonia in right upper lobe. Pneumococcus Type I and Bacillus influenza.

Patient has moved from former address since being discharged and has been lost track of. The question as to whether he ever had any serum sickness following his second pneumonia serum-treatment cannot be answered.

Discussion. Here, then, is a case of recurrent pneumonia Type I, the second attack occurring twenty-nine days after recovery from the first. The infecting organisms may quite possibly have remained in the patient's mouth during the period between the attacks.[14] He was, however, susceptible to a second attack within a month of the first one. To be remembered, in the consideration of this point, is the fact that the first attack was cut short on the third day of the disease by serum treatment. This unquestionably lessened the antigenic value of the first attack and minimized any active immunity which may be acquired in this manner. On the other hand the passive immunity obtained from the horse serum which enabled him to recover promptly from the first attack was not sufficient one month later to protect him from a second attack.

Another interesting phase of this case is the lack of sensitiveness

to horse serum which the patient showed thirty-one days after receiving 100 c.c. of horse serum intravenously.

Longcope and Rackemann[15] in studying 25 cases treated with horse serum made the observations that in cases which escaped serum disease, precipitins and anaphylactic antibodies were not observed, whereas the skin reaction made its appearance irrespective of the amount of serum administered or the method of administration, and appeared whether or not serum disease developed. The skin hypersensitiveness became demonstrable much later, however, in patients who did not develop serum sickness than in those who did, and was first observed in one such case on the thirty-third day and in another on the fiftieth day. They concluded from their observations that serum disease depends on a reaction which takes place within the cells of the body and following which antibodies for horse serum are extruded into the circulation in great quantity. These antibodies dispense with the circulating antigen more or less rapidly.

We see, then, that if serum disease does not develop the circulating antigen may remain for a much longer period and the appearance of circulating antibodies be much delayed or reduced in amount.

Our case differs from their three cases, which escaped serum sickness, in that he did show six days after receiving the first dose of serum a few urticarial wheals. But in view of his subsequent freedom from sensitiveness we feel that it is not safe to place too great reliance on this observation, inasmuch as in the course of making routine ward notes another type of cutaneous lesion may have been mistaken for slight urticaria due to serum sickness. During the twelve days that the patient was under observation following his second course of treatment no sign of serum sickness was noted at any time. No subsequent history is obtainable. We explain his lack of sensitiveness, then, as due to his failure to react in the usual manner by having serum sickness. It is probable that sensitiveness would have developed in a longer period of time.

Conclusions. The development of any active immunity by an attack of lobar pneumonia Type I may be prevented in part or entirely by the early administration of antipneumococcus serum Type I.

Passive immunity obtained from antipneumococcus horse serum Type I may not protect against an attack of pneumococcus Type I pneumonia for more than one month.

Sensitiveness to horse serum is occasionally late in developing; therefore serum treatment of a patient who has recently received serum should not be omitted through fear of anaphylaxis without first testing the patient's degree of sensitiveness and attempting to desensitize him.

It is interesting to note the occurrence of two strongly positive Wassermann reactions, each while the patient's temperature was

up, whereas one done during the afebrile period intervening was negative. In 1918 his Wassermann reaction was positive when he was afebrile.

BIBLIOGRAPHY.

1. Zinsser, H.: Infection and Resistance.
2. Dochez, A. R.: Jour. Exp. Med., 1912, xvi, 665.
3. Chickering, H. T.: Jour. Exp. Med., 1914, xx, 595.
4. Tunnicliff, Ruth: Jour. Infect. Dis., 1911, viii, 302.
4. Weil, Richard: Jour. Exp. Med., 1916, xxiii, 665.
5. Clough, P. W.: Bull. Johns Hopkins Hosp., 1915, xxvi, 37.
5. Strouse, C.: Jour. Exp. Med., 1911, xiv, 109.
5. Weiss, C.: Jour. Med. Research, 1916, xxxiv, 103.
6. Hanes, F. M.: Jour. Exp. Med., 1914, xix, 38.
7. Rosenow, E. C.: Jour. Infect. Dis., 1911, ix, 190.
7. Rosenow, E. C.: Jour. Infect. Dis., 1912, x, 113.
7. Cole, R. I.: Jour. Exp. Med., 1912, xvi, 644.
7. Cole, R. I.: Jour. Exp. Med., 1914, xx, 346.
7. Cole, R. I.: Jour. Exp. Med., 1914, xx, 363.
7. Weiss, C., Kolmer, J. A., and Steinfield, E.: Jour. Infect. Dis., 1918, xxii, 469.
7. Weil, R., and Torrey, J. C.: Jour. Exp. Med., 1916, xxiii, 1.
7. Solis-Cohen, S., Weiss, C., and Kolmer, J. A.: Jour. Infect. Dis., 1918, xxii, 476.
8. Cole, R. I.: Personal communication.
9. Cecil, R. L., and Austin, J. H.: Jour. Exp. Med., 1911, xxviii, 19.
9. Lister, F. S.: Publication of the South American Institute for Medical Research, (quoted by 9), 1916, viii, 1917, x.
10. Blake, F., and Cecil, R. L.: Jour. Exp. Med., 1920, No. 4, xxxi, 403.
11. Neufeld and Händel: Zur Immunitätsforsch., Orig., 1909, iii, 159.
11. Cole, R.: Jour. Am. Med. Assn., 1913, lxi, 663.
11. Avery, O. T., Chickering, H. T., Cole, R. I., and Dochez, A. R.: Monograph of the Rockefeller Institute for Medical Research, October, 1917, No. 7.
12. Dochez, A. R., and Avery, O. T.: Jour. Exp. Med., 1916, xxxiii, 61.
12. Bull, C. G.: Jour. Exp. Med., 1915, xxii, 457.
12. Bull, C. G.: Jour. Exp. Med., 1920, xxxi, 233.
13. Park, W. H., and Biggs, H. M.: Collected Studies from New York State Department of Health, Bureau of Laboratories, 1912–13, vii, 27.
14. Dochez, A. R., and Avery, O. T.: Jour. Exp. Med., 1914, xxi.
14. Dochez, A. R., and Avery, O. T.: Jour. Exp. Med., 1915, xxii, 105.
14. Stillman, E. G.: Jour. Exp. Med., 1916, xxiv, 651.
15. Longcope, W. T., and Rackemann, F. M.: Jour. Exp. Med., 1918, xxvii, 341.

THE COLLOIDAL GOLD CURVE IN EPIDEMIC ENCEPHALITIS: A PRELIMINARY NOTE.*

By Thomas K. Davis, M.D.,

AND

Walter M. Kraus, M.D.,

NEW YORK.

The occurrence of abnormal changes in the reaction of colloidal gold solution to the spinal fluid in epidemic encephalitis has not,

* This paper is based upon cases which have been at Bellevue Hospital, New York, and has been written at the suggestion of Dr. Foster Kennedy, physician in charge of the neurological department. We wish to express our thanks to Drs. Eugene F. DuBois, Robert J. Carlisle, Linnaeus La Fetra, Charles E. Nammack and Van Horne Norris for permission to use reports from their services: We are indebted to Dr. Douglas Symmers for the use of the records of the pathologic laboratory.

Received for publication May 31, 1920.

to our knowledge, been recorded up to the present time. In the course of routine examination of cases of this kind in Bellevue Hospital we have noticed the frequency with which variations have occurred. These variations from the normal suggested syphilis, although there were no other serological (Wassermann) or clinical evidences of this disease. On the other hand there were definite signs of encephalitis of the epidemic type. The spinal fluids upon which these tests were made were sent to the pathologic laboratory, in most cases, shortly after admission. The time of admission varied considerably as regards the week of the disease.

Case No.	Observation.	Weeks.	Cells.	Colloidal gold reaction.
1	1st	I	6	———
2	1st	I	14	1112100000
3	1st	I	40	———
4	1st	II	22	———
5	1st	II	0	———
6	1st	II	23	———
	2d	III	?	———
	3d	V	?	0012210000
7	1st	II	10	0000110000
	2d	V	2	0001121100
	3d	XI	2	4221211000
8	1st	II	0	———
9	1st	II	4	———
10	1st	III	4	———
11	1st	III	43	———
12	1st	III	12	———
13	1st	III	95	0001210000
14	1st	III	43	———
15	1st	III	65	———
16	1st	III	30	———
17	1st	III	134	0012231000
	2d	V	3	———
18	1st	III	20	1122100000
19	1st	IV	9	1222100000
20	1st	IV	?	———
21	1st	IV	10	0000110000
22	1st	V	11	———
23	1st	V	40	0000121000
24	1st	V	5	———
25	1st	V	?	———
	2d	XI	?	———
26	1st	VI	1	———
27	1st	VII	?	5432211000
28	1st	VII	30	0001232100
	2d	XIII	2	5544332100
29	1st	VII	?	———
30	1st	VIII	13	———
31	1st	VIII	19	4432110000
	2d	XII	2	0112210000
32	1st	VIII	8	0122110000
	2d	XVI	4	0022110000
33	1st	XI	14	0000110000
34	1st	XI	?	———
	2d	XII	0	———

NOTE.—Dashes indicate zeros.

The accompanying table indicates the number of observations made, the week of the disease and the number of cells found and the type of colloidal gold reaction. In a few cases more than one observation is recorded. The cases included are not all those admitted to Bellevue Hospital but only those in which colloidal gold tests were done.

In conclusion, we have been unable to observe any relation between the colloidal gold curves noted and the severity, duration or clinical picture of the disease. However, it does appear that in a large percentage (41 per cent.) of cases of epidemic encephalitis chemical changes, whether parenchymatous or meningeal, are present in the central nervous system which produce substances in the spinal fluid able to bring about an abnormal colloidal gold reaction.

It has been shown that in other conditions involving changes in the central nervous system alterations in the reaction of colloidal gold to the spinal fluid are analogous to those just described as occurring frequently in epidemic encephalitis. *Abnormal colloidal gold reactions are evidence of pathologic changes and not of specific etiology.* The diagnosis of etiology by means of the colloidal gold reaction cannot be made without confirming clinical evidence based upon the progress and symptomatology of each case.

CARCINOMA OF THE SUPRA-AMPULLARY PORTION OF THE DUODENUM.

By N. B. Herman, M.D.,

AND

William C. von Glahn, M.D.,

BALTIMORE, MD.

(From the Medical and Pathological Departments, City Hospital, Baltimore, Md.)

Carcinoma of the duodenum may be classified according to position. Clinically the most valuable classifications depend on the relation of the tumor to the ampulla of Vater. Pic[1] speaks of carcinoma of the duodenum as being parapyloric, periampullary or prejejunal. Fenwick[2] and Bland-Sutton[3] classify the growth as supra-ampullary, ampullary or infra-ampullary. The latter grouping is probably the more valuable.

Carcinoma of the duodenum is a rare condition. According to autopsy figures cited by Max Müller,[4] Perry and Shaw,[5] Ruepp,[6] Nothnagel,[7] Tieman[8] and Fritz Müller[9] the average incidence is about 0.035 per cent. Of 4177 cases of carcinoma of the intestine

collected by Jefferson,[10] 130, or 3.1 per cent., were in the small intestine. Brill[11] gives a somewhat lower figure. The proportion of duodenal to jejuno-ileal carcinoma varies with different authors, but a large series of cases show that the two are about equally divided in point of frequency. Involvement of the ampullary region is the most common form of carcinoma of the duodenum; supra-ampullary carcinoma is the next most frequent and infra-ampullary rarest. Averaging the figures quoted by Perry and Shaw,[5] Fenwick,[2] Geiser,[12] Forgue and Chauvin[13] and Rolleston,[14] 24 per cent of duodenal carcinomata occur in the supra-ampullary portion, 64 per cent. in the ampullary portion and 12 per cent. in the infra-ampullary portion.

The relation of supra-ampullary carcinoma to a preceding duodenal ulcer is much disputed. Ewing[15] points out this relationship. Jefferson[10] has collected 30 cases of carcinoma arising in old duodenal ulcers. But certainly carcinoma of the supra-ampullary portion of the duodenum may occur independently of ulcer. Judd[16] says "there is little definite evidence that carcinoma of the duodenum ever arises from an ulcer." Good general reviews of the subject of carcinoma of the duodenum are given by Heulin,[17] Geiser,[12] Deaver and Ravdin,[18] Brill[11] and Forgue and Chauvin.[13] The last two mentioned give very complete bibliographies.

We wish to report the following case:

Charles S., aged seventy-eight years; colored; laborer; admitted on the service of Dr. T. R. Boggs, January 28, 1920. Medical No. 6530.

Complaint. "Sore-mouth; upset stomach."

Family History. Unessential.

Past History. Good general health up to about 1918, when he began to note weakness and lessened ability to work. Constipated since 1918. No melena nor bloody stools. Gonorrhea several times. Genital sore many years ago. No secondaries.

Habits. Unessential.

Weight. Average, 135 pounds. Thinks he has lost 20 pounds in the last year.

Present Illness. Onset about November 15, 1919, with productive cough and weakness. No hemoptyses, but at times there has been blood-streaked sputum. The weakness became progressively more marked until about January 1, 1920, when the patient was forced to take to his bed. There has been fairly constant, slight nausea and for the past two weeks he has eaten very little. Since January 1, 1920, there has been frequent vomiting of small amounts of material; none recognized, however, as food eaten on the previous day. For the two months preceding there had been extreme constipation. No abdominal pain.

Physical Examination. Patient is an emaciated, elderly negro. Teeth represented by a few old snags. Buccal mucosa ulcerated

opposite one such snag. Tongue is heavily coated with a white fur. Breath very foul. No glands palpable above the left clavicle.

Maximal supraclavicular and infraclavicular retraction. Slight respiratory lag over left upper chest. Impairment over both upper fronts, where breath sounds are harsh and expiration prolonged. No rales. In back there is impairment at the left upper shading to almost complete flatness in the left midinterscapular area. Breath sounds here have a distant tubular quality and there are many fine moist rales. Whispered voice accentuated in supraspinous fossa. Heart clear. Slightly increased retromanubrial dulness. Vessel walls markedly thickened, with some calcification. Blood-pressure, 80 to 50.

Abdomen scaphoid. Huge, right inguinal hernia, which has encroached upon the abdominal wall. Abdomen held very rigidly. No tenderness or local spasm made out. Liver and spleen not felt. No masses. At a later examination the patient was put into a warm bath and the abdomen palpated. A sepse of resistance in the epigastrium was made out, but no definite outline could be felt.

Testicles atrophied. No genital scar. Prostate large, soft and homogeneous. Rectum negative.

Ophthalmoscopic examination shows normal fundi.

Laboratory Findings.

Blood. Red blood cells, 3,048,000. White blood cells, 5750. Hemoglobin (Sahli), 45 per cent.

Differential formula showed a slight polymorphonuclear leukocytosis.

Urine. Sp. gr., 1.010 to 1.015. Persistent trace of albumin. Granular casts.

Sputum. Positive for tubercle bacilli.

Stool. Bile present. No ova or parasites. Positive for occult blood. (Benzidine and guaiac tests.)

Test-meal. 100 c.c. of brownish fluid. Bile, 0. Lactic acid, 0. Test for occult blood strongly positive. (Benzidine and guaiac tests.) No Oppler-Boas bacilli. Free HCl, 17 per cent. Combined, 16. Total, 33.

Wassermann. Negative.

Roentgen-ray Report (Dr. J. W. Pierson).

Chest. Marked spotty infiltration, both uppers, more extensive on the left than on the right; tuberculous in origin.

Gastro-intestinal Series. Stomach lies low in the pelvis; marked filling defect in region of antrum pylori, probably due to pressure from lumbar spine; pylorus intact; no retention; duodenal cap well filled. Due to weakness, the patient could not be fluoroscoped.

Course in Hospital. Patient became progressively weaker. He vomited small amounts of fluid material at times. His chief complaint was difficulty in swallowing, but since a stomach-tube passed easily this was thought to be due to a reflex cardiospasm rather than

to an organic esophageal obstruction. On the night of February 10 he showed active delirium. On February 11 he sank into a semicomatose state and died February 12.

Clinical Impression. Ulcerative pulmonary tuberculosis. Carcinoma of the stomach. Secondary anemia.

Autopsy, No. 1592. Anatomic Diagnosis. Chronic fibroid pulmonary tuberculosis, with bronchiectasis; ulcerative tuberculous enterocolitis; conglomerate mass of tubercles in the wall of the aorta; generalized miliary tuberculosis; adenocarcinoma of the duodenum; thrombosis of the right common iliac and right pulmonary arteries, left common iliac vein and prostatic veins; arteriosclerosis; right inguinal hernia; undescended testicle, right; brown atrophy of the heart.

Stomach and Duodenum. The stomach is moderately distended with gas and fluid, especially the pyloric portion. The duodenum, just beyond the pylorus, is enlarged and a dense mass can be felt in it, apparently entirely filling the lumen. The serous surfaces of the stomach and duodenum are smooth and glistening.

When opened the stomach shows no changes. A finger can be readily introduced through the pyloric orifice, but the opening is eccentrically placed and a firm mass can be palpated in the duodenum, completely encircling the finger.

This mass is a large, oblong, solid, polypoid tumor, attached to the inferior wall of the bowel and arising just beyond the pylorus. It measures 6 x 5 x 3 cm. in its greatest diameters. The base is somewhat smaller than this.

The surface of the tumor is smooth and rounded, with small hemorrhages here and there. The upper surface is hollowed out into a deep gutter with steep sides, which gradually taper as they extend upward, and conforming to the curve of the bowel wall they overlap above, forming a tunnel through which the gastric content passed. It was into this tunnel that the finger readily entered. When the bowel was opened these margins sprang apart.

The tumor is grayish white in color and cuts with some resistance. The cut surface is rather homogenous in appearance and is dotted with a few yellow flecks. The growth seems to penetrate only a little way into the wall of the bowel.

The duodenal mucosa is gray and translucent, and is reflected for a short distance upon the base of the tumor. The folds of the mucosa are well defined and prominent. The ampulla of Vater is negative.

The regional lymph glands are not enlarged and there are no metastases visible in the liver.

Microscopic Examination. The tumor is composed of columnar epithelial cells, having a definite glandular arrangement. Often these cells are heaped up into several layers. There is an abundant and rather dense connective-tissue stroma in which are many

capillaries, and which is infiltrated with small round cells, plasma cells and leukocytes. The gland-like spaces enclosed by the epithelial cells are frequently filled with leukocytes. Small areas of necrosis are seen.

At the base the rather orderly adenomatous arrangement is lost, and the cells are more irregular in size and shape and grow in solid cords, penetrating into the circular layer of muscle. Mitoses are fairly numerous. The mucosa can be traced upward upon the tumor for a short distance, then it ends abruptly.

In appearance and arrangement the tumor cells resemble more closely those of the glands of the mucosa than those of Brunner's glands.

In none of the sections of the regional lymph glands could any metastases be found. Sections of the liver and pancreas were likewise negative for metastases.

Discussion. The diagnosis of supra-ampullary carcinoma of the duodenum is surrounded by great difficulties. In fact, Geiser,[12] in 1907, stated that he had been unable to find a case in which the diagnosis had been made *ante mortem*. Most of the cases have been erroneously diagnosed as carcinoma of the pylorus. As can be easily seen, carcinoma at the pylorus and supra-ampullary carcinoma of the duodenum may well give the same symptomatology. Symptoms of weakness, dizziness, emaciation, anemia and the like, referable to the state of carcinoma cachexia, are as common to the two conditions as are the more local symptoms, such as anorexia, flatulence and vomiting. The intestinal symptoms of supra-ampullary carcinoma are not at all typical, melena being the most common. Constipation is the rule. If there is obstruction from either cause there will be dilatation of the stomach and consequent vomiting.

Herz[19] says that the gastric contents in cases of duodenal stenosis, due to supra-ampullary obstruction, are not to be differentiated from the contents in pyloric stenosis. Czygan,[20] however, states that in duodenal stenosis, due to carcinoma, one is liable to get a high HCl content, but he speaks of duodenal carcinoma in general and does not localize the tumor. In the case he cites, one of supra-ampullary involvement, there was 35 per cent. free HCl. Friedrich[21] gives two cases of duodenal carcinoma occurring between the pylorus and the ampulla, where the absence of a palpable tumor and the presence of free HCl led to a preoperative diagnosis of a benign pyloric stenosis. Ewald,[22] Wurm[23] and others cite cases without free HCl and with lactic acid. Friedenwald,[24] in a series of 1000 cases of carcinoma of the stomach states that 89 per cent. show an anacidity and a further 3 per cent. show a hypochlorhydria; 82 per cent. show lactic acid. This author also points out that anacidity is an early finding in gastric carcinoma. Although no hard and fast rule can be laid down as to the presence of free HCl in the gastric contents in cases of supra-ampullary duodenal carci-

noma, it seems safe to conclude that the HCl disappears much earlier in cases of gastric carcinoma than in cases of neoplasm of the duodenum.

Forgue and Chauvin[13] mention that blood is infrequently found in the gastric contents in cases of duodenal cancer while it is a very common finding in gastric carcinoma. A high grade of indicanuria has been said to be of some help in the diagnosis of duodenal carcinoma if the lumen of the duodenum is occluded.

Pain is an extremely variable symptom, both as to presence and as to location. It usually is not a prominent feature. If present it is more often of a constant, dull, dragging quality, usually referred to the epigastrium. It is more liable to have no relation to meals. The pain may sometimes be paroxysmal in character, due presumably to sudden changes in the degree of distention of the gall-bladder. According to Geiser,[12] icterus may occur as a late manifestation in supra-ampullary carcinoma even though the ampulla be not directly involved.

Most authors agree that the tumor is seldom palpable, although Fenwick[2] claims that in 60 per cent. of the cases the mass can be felt if it is located near the pylorus. Rosenheim[25] states that supra-ampullary carcinoma of the duodenum, if to be felt at all, is to be sought for just a little to the right of the midline and on a sector between the umbilicus and the gall-bladder region. Forgue and Chauvin[13] explain the rareness of a palpable mass on the basis of the form of duodenal carcinoma. Carcinomata of the duodenum are usually either flat plaques, showing a tendency to annular growth, or are nodules so small that they escape palpation. Judd[16] also points out that duodenal carcinomata are often polypoid in character. What has at times been taken for the primary mass on palpation has later been seen to represent a group of metastases in mesenteric glands. Duodenal carcinoma, in general, does not metastasize readily or early. The most common sites of metastases are in the pancreas, the liver and glands. Enlargement of the supraclavicular glands, especially on the left, have been described, as well as metastases to the vertebræ. The nodules in the liver seldom attain any great size.

From the roentgen-ray standpoint, carcinoma of the duodenum is an almost unknown occurrence. Dr. F. H. Baetjer[26] has told us that he has never seen a case. Carman and Miller[27] do not mention duodenal carcinoma as such. They say: "Other than duodenal ulcer the only important condition of the small intestine which is readily susceptible of demonstration by the roentgen-ray is obstruction; if near either extremity of the bowel the site of the obstruction can be shown." They give no pertinent picture, however. Judd[16] from the same clinic gives a number of pictures of intestinal obstruction but none would allow of a definite diagnosis of duodenal carcinoma. There was no obstruction in our case. Clinically

the gastro-intestinal roentgen-ray series was essentially negative, although at the time the length of the "stalk" of barium (*C* in Fig. 1) was commented on. This was taken to be the stream of barium passing through the pylorus. The duodenal cap (*D* in Fig. 1) was

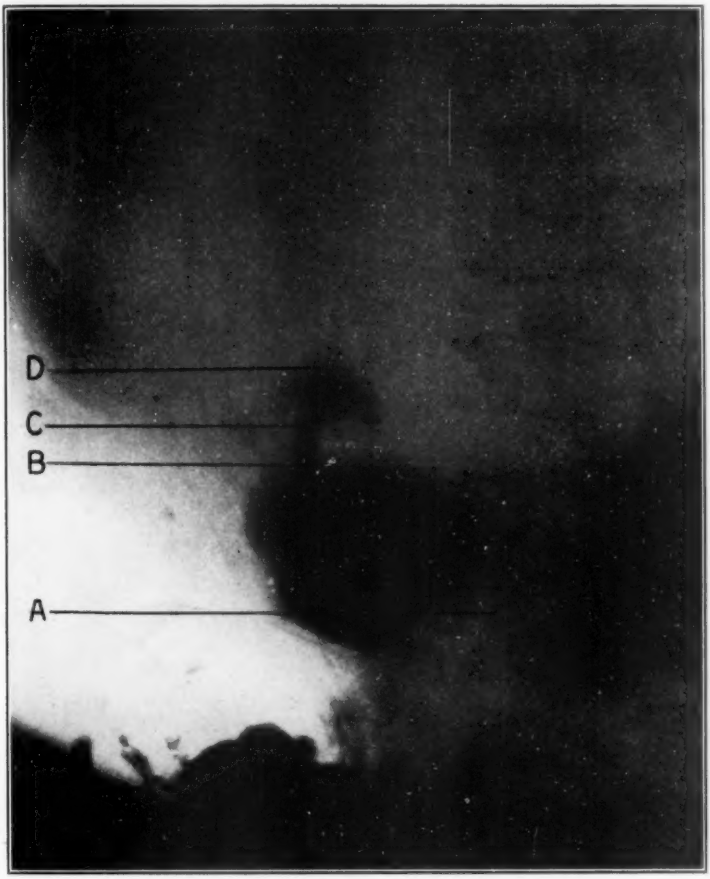


FIG. 1.—Roentgen ray of stomach fifteen minutes after ingestion of opaque meal. *A*, filling defect due to pressure of spine; *B*, pylorus; *C*, stream of barium passing through the lumen formed in the carcinoma; *D*, duodenal cap.

normal. On comparing the roentgen-ray picture with the pathologic specimen the real explanation became apparent. The carcinoma had formed a canal, as it were, through which the gastric contents passed, and this "stalk" represented the stream of barium passing through the lumen of the duodenal growth. Several small, soft

FIG. 2.—Adenocarcinoma of the duodenum. Note the deep gutter on the upper surface of the tumor. *P*, pylorus; *V*, ampulla of Vater.

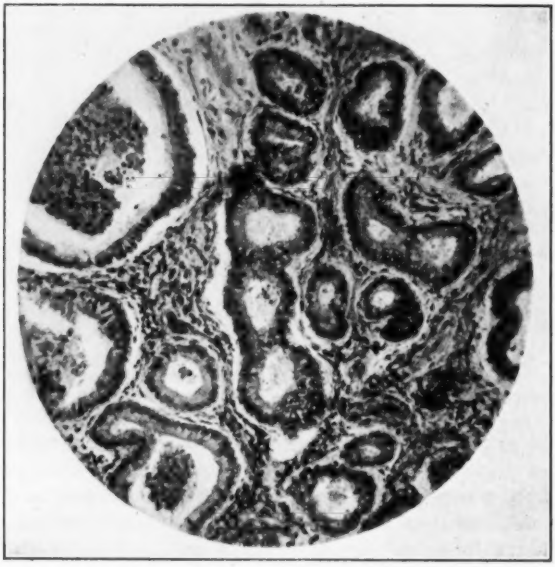


FIG. 3.—Adenocarcinoma of the duodenum. Section showing type and characteristic arrangement of tumor cells and abundant stroma. ×125.

shadows surrounding the stalk are probably due to leakage of barium between the mass and the duodenal wall, since the sides of the carcinoma did not fuse above. This roentgen-ray finding has been thought to be conclusive enough to warrant a strong suspicion of duodenal carcinoma in case another similar picture should present.

Conclusions. The rarity of duodenal carcinoma has been pointed out and the difficulties of diagnosing this condition, when it occurs in the supra-ampullary portion, have been outlined. The persistence of free HCl in the gastric contents, when all other evidence points to a gastric carcinoma, should make one at least think of duodenal carcinoma. In the light of the pathologic findings we believe that a similar roentgen-ray picture, in the future, will strongly suggest a carcinoma of the supra-ampullary portion of the duodenum.

We are indebted to Dr. E. H. Terrill for the photograph of the tumor and for the photomicrograph.

BIBLIOGRAPHY.

1. Pic, A.: Revue de Méd., 1894–1895.
2. Fenwick: Edinburgh Medical Journal, 1901, x, 309.
3. Bland-Sutton: Tr. Med. Soc., London, 1914–1915, xxxviii, 1.
4. Müller, Max: I. D. Bern, 1892. Quoted by Geiser.
5. Perry and Shaw: Guy's Hosp. Rep., 1893, p. 274.
6. Ruepp: I. D. Zürich, 1895. Quoted by Geiser.
7. Nothnagel: Die Erkrank. des Darms, Vienna, 1898.
8. Tieman: I. D. Kiel, 1900. Quoted by Geiser.
9. Müller, Fritz: I. D. Basel, 1905. Quoted by Geiser.
10. Jefferson: British Jour. Surg., 1916–1917, iv, 209.
11. Brill: Am. Jour. Med. Sc., 1904, cxxviii, 824.
12. Geiser: Deutsch. Ztschr. Chir., 1907, lxxxvi, 41.
13. Forgue and Chauvin: Rev. de Chir., 1914–1915, l, 470.
14. Rolleston: Lancet, 1901, i, 1121.
15. Ewing: Neoplastic Diseases, Philadelphia, 1919, p. 640.
16. Judd, E. S.: Journal Lancet, 1919, xxxix, 159.
17. Heulin: Thèse, Paris, 1897.
18. Deaver and Ravdin: Am. Jour. Med. Sc., 1920, clix, 469.
19. Herz: Deutsch. Med. Wchnschr., 1896, xxiii, 362.
20. Czygan: Arch. f. Verdauungskr., 1898, iii, 82.
21. Friedrich: München. med. Wchnschr., 1904, p. 2073.
22. Ewald: Berl. klin. Wchnschr., 1886, p. 527.
23. Wurm: I. D. Munich, 1902.
24. Friedenwald, J.: Am. Jour. Med. Sc., 1914, cxlviii, 675.
25. Rosenheim: Path. und Ther. der Krankh des Darms., 1893, p. 450.
26. Baetjer, F. H.: Personal communication.
27. Carman and Miller: The Roentgen Diagnosis of Diseases of the Alimentary Canal, Philadelphia, 1917; p. 429.

ETIOLOGY OF ACNE ROSACEA THROUGH A VISCERO-NEUROLOGIC MECHANISM.

By Frank Porter Miller, M.D.,
LOS ANGELES, CALIF.

The causation of acne rosacea as well as many of the other common dermatoses has been more or less a matter for conjecture. So many predisposing factors have been ascribed, and these so variable, that no tangible etiology has been forthcoming. Heretofore any skin disorder without an apparent etiology has been classed as being of a nervous origin, but as our neurologic knowledge increases and becomes more precise, we are able to eliminate a few in the group of the so-called nervous dermatoses.

Disturbances of the peripheral mechanism of vasomotor pathways have been analyzed in a few diseases, including tonic hyperemias (erythromelalgia), a few of the spastic anemias, such as Raynaud's disease, intermittent claudication and vasomotor irritability, as in acute angioneurotic edema, and multiple gangrene of the skin.

The cutaneous disorders offer a lucrative field for investigation, and many etiologic factors which have been clouded with obscurity will unfold if we possess an adequate knowledge of visceral neurology.

For the sake of clarity and also for completeness, I will review the prevailing etiology and symptomatology in as brief a manner as possible. This is essential if the reader is to get a comprehensive conception of our explanation.

Acne rosacea consists of two processes, a rosacea and an acne. The former is a chronic, congestive disorder of the face, particularly of the nose, chin and forehead, characterized successively by flushing, permanent enlargement of the bloodvessels, and in some advanced cases, tissue hypertrophy (rhinophyma). The acne lesions are usually secondary in development. There are essentially three stages of the disease; the first manifestation is a tendency to flushing of the face, which becomes especially evident after eating or drinking stimulating articles or exposure to cold wind or upon entering a warm room. There is a distinct predilection for the middle third of the face, but in the majority of cases the malar regions are also involved. The redness is usually transitory at first. In many cases the condition passes on to the second stage. The frequent repetition of flushing gradually tends to enlargement of the capillaries and venules which now become visibly dilated. They are seen as small tortuous or arborescent vessels on the nose and cheek. The appearance commonly described as brandy nose is now present. Coughing, laughing and mental excitation lead to paroxysmal exacerbations. Acne papules and pustules now usually make their appearance in crops. In exceptional cases the

disease progresses to the third stage, which is characterized by further capillary engorgement and tissue hypertrophy.

Gastro-intestinal disorders, improper diet, inordinate use of tea and coffee and alcoholic beverages, have all been suggested as predisposing factors. Although most dermatologists realize there is a neurogenic element which masks the etiology, the anatomic pathways have never been suggested.

There is no true acne rosacea, as we will attempt to prove in the following paragraphs, and to get the correct conception we will discuss this from a polyetiologic viewpoint.

Vagal and Trigeminal Stimulation. It is universally accepted that gastric stimulation is probably the causative factor in a great majority of cases, and when the stimulation is great enough to evoke a response, the afferent sensory impulse courses through the vagus, the cells of which are situated in the ganglion nodosum and thence to that portion of the dorsal nucleus receiving the visceral fibers. Interconnecting neurons now communicate with the nucleus of the fifth cranial and by antidromic impulses vasodilatation is produced. It has been shown by Stricker and Morat[1] that dilatation of the vessels of the hind limb can be produced by stimulating the posterior roots of the nerve going to the limb, *i. e.*, far below the point of origin from the cord of the constrictor fibers to the same part of the body. This work was widely discredited until later confirmed by Bayliss[2] for all manner of stimuli. He has shown that stimulation of the posterior roots either before or after they have passed through the ganglia causes dilatation of the vessels in the area of the supply of the roots, whatever be the nature of the stimulus employed, whether electric, chemical or mechanic. This effect is not destroyed by previous section of the posterior roots on the proximal side of the ganglia, showing that the fibers by means of which the dilatation is produced have the same origin and course as the ordinary sensory nerves of the limbs. Since the vasodilator impulses pass along these nerves in a direction opposite to that taken by the normal sensory impulse, Bayliss has designated them as antidromic impulses. In accepting this view we must assume that stimulation of any of the sensory nerves of the body is capable of producing vasodilatation, and sensory nerves are capable of carrying efferent impulses. It is quite possible that antidromic impulses could explain many of the trophic disturbances in dermatalogy. Since the above holds true for stimulation of the posterior roots of a spinal nerve we have every reason to believe that the same would be applicable in the sensory division of the fifth cranial, as the spinal nerves and the trigeminus have many characteristics in common. Both possess a motor as well as a sensory root. The fibers of the sensory root take their origin from the Gasserian

[1] Starling: Human Physiology, Lea & Febiger, 1915, p. 998.
[2] Ibid., pp. 998–999.

ganglion, which is in all respects similar to the ganglion of a posterior spinal nerve root. The afferent fibers of the fifth nerve, as they enter the pons, bifurcate like a spinal afferent nerve into ascending and descending branches. Furthermore the sensory portion of the fifth nerve bears the same relationship to the parasympathetic system as the spinal nerves do to the sympathetic.

Gaskell[3] accepts the presence of vasodilator fibers in sensory nerves with considerable hesitancy and suggests that sensory fibers probably possess secretory functions. His reasoning is very plausible, and we will produce it in part. The condition of the epithelial cells of the skin is dependent on the integrity of the sensory nerves. Therefore the sensory nerves affect the metabolism of the cutaneous epithelial cells. When the secretory nerve to a gland, such as submaxillary gland, is cut the gland cells atrophy, and when sensory nerves to the epithelial cells have been sectioned, atrophy and glossy skin result. The sensory nerve may be considered to control the metabolism of epithelial cells in a manner exactly comparable to the control of gland cells by their secretory nerve. Stimulation of the chorda tympani causes secretion, and that secretion is accompanied by dilatation of the bloodvessels of the gland, probably due to acid metabolites. This is an acid lymph acting upon the loose adventitia of the small vessels. If stimulation of the sensory nerve causes metabolic changes in the epithelial cells corresponding to those in the submaxillary glandular cells upon stimulation of the chorda tympani, then the formation of acid metabolites would cause dilatation of the bloodvessels of the skin just as in the case of submaxillary bloodvessels. From the physiologic data it is shown that stimulation of any sensory nerve is capable of producing a vasodilatation, but whether the impulses are carried through true vasodilator fibers, acting antidromically, or the sensory nerves assume secretory characteristics, is a matter for physiologists to decide.

This shows that the law of Bell and Magendie is not infallible and offers one of the exceptions to the universal law of forward direction in the mammalian nervous system.

Pottenger[4] has recently explained hectic flush as it occurs in respiratory diseases through this mechanism, though the manuscript is as yet unpublished, he is kind enough to allow me to quote from it. In cases of pulmonary tuberculosis the stimulation does not limit itself wholly to the area supplied by a fifth cranial, but here we also have stimulation from a sympathetic origin. The afferent impulses from the lung mediate with the cervical spinal nerves particularly the third and fourth segments, and by stimulating the third cervical the pinna of the ear will develop a flush, and in a few cases will become noticeably larger than the opposite organ. The flush as it occurs in the malar region is a vagal-trigeminal mediation.

[3] Involuntary Nervous System, 1915, pp. 96–97.
[4] Unpublished manuscript.

Local irritation of the peripheral fibers of the fifth nerve will produce the flush, and it is immaterial whether the stimulation arises from within or without the body. The sensory receptors of the trigeminus are widely distributed over the face, the mucous membranes of the superior and anterior nasal fossa, the frontal and ethmoid sinuses, tentorium cerebelli, teeth, mucosa of the posterior inferior nares, the sinuses of the jaw, dura mater, the mucous membrane of the lips, cheeks, posterior and inferior portion of the mouth and the anterior two-thirds of the tongue as taste buds. It is quite conceivable to me that stimulation of these peripheral fibers over a prolonged period would produce a typical acne rosacea. The warmth of a room is often sufficient to bring this out in many individuals, and in others the slightest friction over the sensory fibers will produce the blush.

Since the physiologists have laid so much stress upon the fact that certain impulses will produce an inhibition of the vasoconstrictor center, I will mention another pathway here, though realizing the probability of its occurring in this instance is quite remote. The afferent sensory impulses course centralward until they reach the medulla and then by intercalated neurons are transferred to the vasoconstrictor center producing inhibition. The vasoconstrictor center sends axones via the descending tracts in the cord which terminate at various levels in the anterior horn of the gray matter in the region from the upper thoracic to the upper lumbar spinal nerves. We also know that in the cervical portion of the sympathetic, dilator fibers are carried which are distributed to the mucous membrane of the mouth (lips, gums and palate) nostrils and the skin of the cheek. These fibers, passing from the vasoconstrictor center, pass as pre-ganglionic fibers to the superior cervical ganglion, and thence as postganglionic fibers to the Gasserian ganglion and are distributed to the buccofacial region in the branches of the fifth cranial nerve.

Psychical Relationship. The psychical side of medicine has been sadly neglected; and because of our indifference, or rather our inability to fathom this particular phase, many new cults have attempted to bridge the space which should have been spanned by medicine, and the laity only too eager to accept a new code have been misled, although these cults smack strongly of quackery. Especially those individuals suffering from some chronic disorder, in which the progress has been slow, or the result ungratifying, have been prone to adopt a new creed and the harm resulting from such a reprehensible practice is rather alarming.

The activity of the psychical centers is particularly interesting in acne rosacea, and it is through their activity that the physiology of blushing is explained; and blushing which is produced by the slightest provocation forms one of the early symptoms of the disease, frequent repetition producing enlarged bloodvessels and

finally tissue hypertrophy. Although the location of the psychical centers is rather indefinite it is assumed that they are located in the midbrain or cortex. When feelings of embarrassment or shame are thrust upon an individual the impulse is transmitted to the psychical centers, thence by intracentral nerve paths, which communicate with the sensory nuclei or the trigeminus, producing a reflex vasodilator effect in the area supplied by the fifth cranial. Concomitant with the phenomena of blushing, other functional disturbances are observed, and these are quite constant in all the emotional states of a depressing nature (mydriasis, hyperidrosis, cardiac palpitation and dryness of the mouth and throat). The act of blushing, apparently simple, resolves itself into an intricate mechanism, and by secondary connector neurons stimulates the respiratory center in the medulla, and by the aid of descending tracts in the cord the motor cells in the sympathetic ganglia of the cervical regions are implicated and mydriasis and palpitation occur. It is impossible to decipher with any degree of certainty the mechanism which is conducive to an emotional state, but it is well to remember that the changes may be of a biochemical nature involving the cells of the cerebral cortex. It has been suggested to me that acne vulgaris could probably be explained in a similar manner and that the awakening of sexual desires at puberty produces a reflex stimulation from the cortex to the sensory nuclei of the trigeminus, and that hypernutrition causes an enlargement of the sebaceous glands. This is a suggestion worthy of thought; but remembering that the endocrine glands probably play a leading part in this particular role, it should be borne in mind that when an impulse reaches the brain or spinal cord there are certain neurons which are more direct and offer less resistance than others, and it is along these paths that the reflex will take place; and we may further assume that these paths of least resistance, as they have been called, are in part preformed and in part laid down by the repeated experiences of the individual, and many of these cases which in the beginning show a transitory flush, easily provoked, will in time assume a permanent reddish hue if stimulation is continued.

Furthermore, I am of the opinion that many of these people possess a tricotonic instability. For quite a period clinicians have accepted vagotonia as a distinct entity, and in this condition I believe we probably have an increased tonus and a lessening of the threshold of response in the trigeminus.

Very little has been said regarding the acneiform eruption, but its presence has been explained for a long period as being due to hypernutrition and is merely secondary manifestation.

REVIEWS

Diseases of Children. By John Lovett Morse, M.D., Professor of Pediatrics, Harvard Medical School; Visiting Physician at the Children's Hospital and Consulting Physician at the Infant's Hospital and at the Floating Hospital, Boston. Third edition. Pp. 639; 200 case histories, freely illustrated. Boston: W. M. Leonard, 1920.

The third edition has been thoroughly revised, but the general plan of presenting the subject through the medium of the histories of actual cases has been retained. Many new cases have been substituted for old ones and in others the diagnosis and treatment have been formulated on more modern lines rather than detailing those that were actually employed. The whole subject of pediatrics is well covered under the usual classification, with a final section for the more rare conditions which do not fall definitely under the "system diseases." This type of book offers one of the best means for practitioners to develop their powers of inductive reasoning, if they will avoid reading the final conclusion until after they have attempted to draw their own inferences. Most noteworthy is the fact that the author reaches his diagnosis chiefly with the aid of clinical observation at the bedside. Nothing could better illustrate the value of trained observation and careful physical diagnosis as contrasted with the too prevalent modern tendency to rely too largely upon laboratory aid, valuable as the latter undoubtedly is.

J. C. G.

An Atlas of the Primary and Cutaneous Lesions of Acquired Syphilis in the Male. By Charles F. White, M.B., Major, R.A.M.C., Rochester Row Military Hospital, and W. Herbert Brown, M.D., late Captain, R.A.M.C., Victoria Infirmary, Glasgow. First edition. Pp. 32; 79 illustrations (photographic) and 4 colored plates. New York: William Wood & Co., 1920.

An atlas founded upon 19,000 cases of syphilis studied and photographed in a large army venereal hospital. Nine thousand cases of primary sores gave the authors the material to classify ten different types of chancre; a classification entirely new, true to

experience and a welcomed change from text-book reiteration. The idea of making many (51) of the photographs for stereopticon study is novel and highly instructive. The text is brief, succinct, and descriptive, being limited to only an accurate picture of the various lesions, in which you can feel the authors speaking from close personal observation. One hundred and thirty extragenital chancres are studied. In each lesion described the percentage of the frequency of its occurrence is stated, being most valuable as coming from such a large personal series. A. R.

INDEX OF SYMPTOMS. By RALPH WINNINGTON LEFTWICH, M.D., Late Assistant Physician to the East London Children's Hospital; Author of "Tabular Diagnosis," etc. Seventh edition, revised by H. N. WARNER COLLINS, B.Sc., M.R.C.S., L.R.C.P. Pp. 595. New York: William Wood & Co., 1920.

THE seventh edition of Leftwich's work has been revised by Collins. The latter has added considerable material to the work so that the present edition is a distinct improvement over former ones. The reviewer finds that as compared with the second edition nearly 200 additional pages have been incorporated in the text. To those who are not familiar with the book, or books of this type, it may be said that symptoms and signs are listed under the various main headings of physical diagnosis. Under these main headings are subheadings of the symptoms relating to the main heading. After the symptoms, in alphabetical order, are arranged the diseases which will produce this symptom. The ones most likely to cause the symptom are starred. In this way one is able to arrive at a diagnosis by methods somewhat different from the ordinary ones in common use; thus if we find that a patient has pain in the chest we look under this heading and find the list of diseases which are associated with pain in the chest. Then we find that he also has cyanosis. The heading cyanosis is consulted and all diseases which are not associated with pain in the chest and with cyanosis are eliminated, while tabulating the diseases which are associated with these two symptoms, pain in the chest and cyanosis. We then take up a third and fourth symptom which the patient presents and tabulate those diseases in which all four symptoms are present. Continuing in this manner indefinitely until we have ruled out all diseases which are not listed under the heading of the symptoms the patient presents we can ultimately arrive at a diagnosis, presumably with a minimum of trouble. The method sounds attractive and easy, but unfortunately it is not always easy to interpret physical signs or properly to evaluate accurately, subjective symptoms described by the patient. J. H. M., JR.

EATING TO LIVE LONG. By WILLIAM HENRY PORTER, M.D. Pp. 243. Chicago: Reilly & Lee Company, 1920.

THIS small volume contains twenty-two chapters on various subjects connected with food and diet. The author discusses foods from every standpoint. He explains to us what foods are good and what foods are bad and he gives adequate reasons for his views. Furthermore, he dismisses with a thorough explanation the fallacies of some of the various dietetic delusions with which this subject has been burdened in the past.

The book is written in such a manner as will appeal not only to the physician but will also be classed among the popular medical books which may be read by the layman with interest, not to mention the benefit that he would derive from a study of the context.

J. H. M., JR.

INTERNATIONAL CLINICS. By H. R. M. LANDIS, M.D. Thirtieth series. Pp. 314; 40 illustrations. Philadelphia and London: J. B. Lippincott Company, 1920.

VOLUME II of the thirtieth series of these clinics contains eighteen articles on subjects of varying interest. The clinics are interesting and well worth reading. Particular commendation should be given the clinics of Drs. Ashhurst, Thompson, Lyon, Magnuson and Speese. They are well written and authoritative.

J. H. M., JR.

THE DUODENAL TUBE AND ITS POSSIBILITIES. By MAX EINHORN, M.D., Professor of Medicine at the New York Postgraduate Medical School; Visiting Physician to the Lenox Hill Hospital, New York. Pp. 122; 51 illustrations. Philadelphia and London: W. B. Saunders Company, 1920.

DR. EINHORN, in this little work on the duodenal tube, first traces how he developed this instrument from its original model to its present finished state. He then shows for what purpose it may be employed in diagnosis of diseases of the upper alimentary tract, and lastly concludes his work with several chapters on the use of the tube in the treatment of diseases in this part of the body. Full credit should be given to Dr. Einhorn for his development of this device which has proved so useful in diagnosis, and which is so very extensively employed in the present day. It hardly seems fair that more credit is not given to Dr. Einhorn for conceiving, developing and popularizing the tube. Minor modifications in the shape of

the capsule have been made by other individuals which in no way alter the principles of the tube, and because of these minor modifications, the name of the modifier has been applied to the tube as a whole, although these changes have in no sense altered the basic principles of the instrument. J. H. M., Jr.

Surgical Clinics of Chicago. October, 1920. Vol. IV, Number X. Pp. 223; 46 illustrations. Philadelphia and London: W. B. Saunders Company.

This number continues the character of work and good reputation of the *Clinics*. It has broadened its scope and increased the number of its contributors, giving the reader articles on the specialties in medicine and surgery. So that there is valuable reading for most of the medical profession.

The case reports are most admirably worked up, and the minutest details presented. In fact the one criticism is that possibly in some instances a little too much space is given to remote family and personal history. The articles on perinephric abscess, lesions, transfusion, kidney infections and hematuria, will be of interest to all surgeons. E. L. E.

Mental Deficiency (Amentia).[1] By A. F. Tredgold, M.D., F.R.S., Edin. New York: William Wood & Co., 1920. Third edition.

This is the third edition of this very important work, and has been thoroughly revised and brought up to date, the chapter on Moral Imbecility having been entirely rewritten. With the exception of this chapter there is no marked difference from the former editions.

From the medicolegal standpoint the chapter on Vicious and Criminal Aments and the following chapter on Moral Imbecility are most satisfactory, for they clarify this very important subject. According to the author, in vicious and criminal aments there is a fundamental inability to develop a moral sense, with the result that serious misconduct is characteristic of their lives. In another type of aments the misconduct is due to weakness of will. The third type consists of those who suffer from morbid impulses. He calls attention to a residue of criminal aments who cannot be thus precisely docketed, for their misconduct depends upon a combination of defects. In many the early upbringing is at fault, for the qualities of moral sense and inhibition have never been developed. In discussing the moral imbecile, the author properly points out that

one reason for the misconception of this group of cases is because the term "imbecile," which has long been applied to an immense degree of mental defect, is entirely unlike that present in these cases. For this reason he prefers the term moral "defective." The best definition of a moral imbecile is that given by the author when he says "these individuals have defective wisdom, with a defect of moral sense." He further points out that moral imbeciles are by no means unintelligent in the ordinary sense, and re-emphasizes the fact that these patients are clever but incapable, that they may have plenty of intelligence but little or no wisdom, and that, as Dr. Mercier pointed out, such an individual is a "clever fool."

Another chapter upon The Criminal Responsibility of Aments is also very instructive. Altogether this is an excellent book.

PHYSICAL BASIS OF HEREDITY. By THOMAS H. MORGAN, Professor, of Experimental Zoölogy in Columbia University. Pp. 305; 117 illustrations. Philadelphia and London: J. B. Lippincott Company.

OF the recent advances in the study of heredity and Mendelism none have been so productive in results as the experimental work of Professor Morgan and his colleagues. About ten years ago they began work with Drosophila, the little fruit fly, and this form has turned out to be the most favorable yet utilized in the study of heredity. In Drosophila they have already found several hundred factors which exhibit Mendelian segregation; its chromosomes are distinct and few in number; it is both hardy and prolific; it is easily handled in the laboratory, being reared in pint bottles and fed on small pieces of ripe fruits. These advantages have been utilized to the full and the author believes that, as a result, some of the basic problems of heredity have been solved. In fact the opening statement in this book is: "That the fundamental aspects of heredity should have turned out to be so extraordinarily simple, supports us in the hope that Nature may, after all, be entirely approachable. Her much advertised inscrutability has once more been found to be an illusion due to our ignorance." The book deals with both genetics and cytology and the main thesis is the chromosome theory of heredity. According to this the chromosomes form the material basis of heredity. The various factors, upon which the manifestations of characters depend, are resident in the chromosomes, whence they influence the nature of the cells and of the organism which the cells collectively build up. The six principles of heredity are discussed in the light of our present knowledge of the chromosomal mechanism.

Due recognition is given the valuable work of Carothers on the mechanism of assortment and that of Wenrich on crossing-over and the linear order of the material of the chromosomes. The involved portions of the discussion will appeal more to the specialized student of this subject, but there is much of interest to the general scientific reader. Those interested in the study of genetics will look forward to reports of the work being done this year in California by Professor Morgan and his associates.

W. H. F. A.

THE NATURE OF ANIMAL LIGHT. By E. N. HARVEY, PH.D., Professor of Physiology, Princeton University. Pp. 182; 35 figures. Philadelphia and London: J. B. Lippincott Company, 1920.

ONE of the first questions asked the author when discussing the nature of animal light is whether it is likely ever to be used for commercial purposes. In spite of the negative answer to this inquiry there are other interesting points of view from which the subject will continue to be studied. The historic sketch of early observations of these phenomena, though short, is full of interest. Aristotle's name which is at the beginning of every science, appears also in this. In the days of "laudable pus," wound-infection by luminous bacteria, which caused the wounds to glow at night, was rather welcomed by surgeons. In the animal kingdom there are at least thirty-six orders known to produce light, and two groups among plants. The light is of the nature of luminescence, *i. e.*, its emission is stimulated by some other means than heat. After chapters on luminescence and incandescence, physical nature of animal light and structure of luminous organs, follow two chapters on the chemistry of light production. In these the properties of the three principal substances concerned in this phenomenon, luciferin, oxyluciferin and luciferase, are discussed at length and the author gives the results of his own studies. W. H. F. A.

DAS GESCHLECTSLEBEN DER NATURVOELKER. By H. FEHLINGER. Pp. 93; 9 illustrations. Leipzig: Curt Kabitzsch, 1920.

THIS little paper-bound brochure is a monograph devoted to the consideration of the sexual life and customs of aboriginal people. The topics considered include the attitude of these people toward nakedness, prenuptial freedom and marital fidelity, courtship, marriage, childbirth and induction of abortion, the ignorance on the subject of generation, disfiguration of the genital organs,

sexual maturity and the post-sexual life. It is illustrated by means of some very interesting actual photographs of savage people, showing the lack of body covering prevalent in such tribes. The article is written in a very interesting style and the previous literature on the subject is freely quoted. It should be of interest to students of eugenics. F. B. B.

EXOPHTHALMIC GOITER AND ITS NON-SURGICAL TREATMENT. By ISRAEL BRAM, M.D., Instructor in Clinical Medicine, Jefferson Medical College, Philadelphia; Physician on Visiting Staff of Philadelphia General Hospital; Member of the Society for the Study of Internal Secretions, Etc. Pp. 438. St. Louis: C. V. Mosby Company, 1920.

COMING at a time when the surgical treatment of exophthalmic goiter seems to be on the defensive, any book on the non-surgical treatment of this disease is of noteworthy interest. Coming in a day when surgery claims so much and sensationally holds the therapeutic field, the author of this work is to be congratulated upon his daring to claim openly anything whatever for medical treatment. We believe that hyperthyroidism properly belongs in a majority of cases to non-surgical therapeutics, but we are rather disappointed that no stronger case against the scalpel has been made out by the writer's experience.

Eight case histories with their physical examinations are presented as being "illustrative of the potentiality for cure of exophthalmic goiter by non-surgical means." There are no records of laboratory work included in the histories, and nothing is said of metabolic studies. One of these cases was treated by mail and was never seen by the author.

In addition to these cases "selected at random" two chapters are devoted to the anatomy and physiology of the thyroid. Other chapters are given over to the pathology, pathogenesis, symptomatology, diagnosis, prognosis and non-surgical treatment of exophthalmic goiter. Some of the chapters are with few changes the author's reprints of articles published elsewhere in the literature. Such a chapter is the one on Shell Shock (?) in Soldiers.

The chapter on therapeusis is interesting, but offers no new ideas on treatment. Most of the suggestions have been used for a long time and are such as have yielded results for many men in some cases of toxic goiter. In other parts of the book much of the general literature on this endocrine dysfunction is utilized as a background, and in this way its non-surgical aspects are well supported.

The nature of endocrine disturbances *a priori* always leads to differences of opinion, theorization and questionable conclusions.

There seems to be no doubt in the author's mind that proper medical care of thyroid intoxication will yield 100 per cent. cures. We should be surprised to see some cases of exopthalmic goiter yield to any sort of therapeutic procedure.

We must, however, again congratulate the writer on calling attention to the fact that medical procedures in exophthalmic goiter are not without results if the patient is not too toxic and can economically devote enough time to the treatment. T. G. S.

MARINE HYGIENE AND SANITATION. By GILBERT E. BROOKE, M.A. (CANTAB.), L.R.C.P. (EDIN.), D.P.H., F.R.G.S., Chief Health Officer, Straits Settlements Medical Department, Port Health Officer, Singapore; Lecturer in Hygiene to Singapore Medical School; author of "Tropical Medicine, Hygiene and Parasitology," "Essentials of Sanitary Science," "Aids to Tropical Medicine," etc. First edition. Pp. 402; illustrated. New York: William Wood & Co., 1920.

THE author aimed to write a handy, practical manual of "sailing directions," and has succeeded. This book is the outgrowth of everyday experiences.

The introductory chapter on the ship's surgeon deals with the growth of the idea of using medical men on men-of-war and merchant ships, a practice dating back to about 1600.

The chapter on the structure of ships, with its glossary, is a necessary forerunner of the subjects of ventilation, fumigation and extermination of vermin. When one counts in the pages on this topic seven species of the rat family, at least fifteen species of fleas, several species of bed-bugs and eleven tribes of cockroaches, "all of which may be found on ships trading between Europe and the tropics," one has a more kindly feeling toward the executive officer of such old ex-commerce destroyers as the "De Kalb."

There is practical advice on the watering the victualling of ships, on quarantine inspection, on ship-borne infections and how to handle them, and on sanitary inspection and disinfection of ships.

There are articles on port health officers, light-houses, light-ships, dietetic schedules, supply table lists, signal codes, etc.

The rulings of the Inter-Sanitary Convention, Paris, 1911–1912, concerning plague, cholera and yellow fever, appear in an appendix. One feels that this manual is a mine for the naval reservist of the medical corps, for those entering the medical service of the merchant marine, and also that it contains many practical suggestions and reference tables useful to the experienced sea-goer. J. E. T.

PROGRESS
OF
MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF

W. S. THAYER, M.D.,

PROFESSOR OF CLINICAL MEDICINE, JOHNS HOPKINS UNIVERSITY, BALTIMORE, MARYLAND,

ROGER S. MORRIS, M.D.,

FREDERICK FORCHHEIMER PROFESSOR OF MEDICINE IN THE UNIVERSITY OF CINCINNATI, CINCINNATI, OHIO,

AND

THOMAS ORDWAY, M.D.,

DEAN OF UNION UNIVERSITY (MEDICAL DEPARTMENT), ALBANY, N. Y.

A Study of the Correlation of the Basal Metabolism and Pulse-rate in Patients with Hyperthyroidism. — STURGIS and TOMPKINS (*Arch. Int. Med.*, 1920, xxvi, 467) report on 99 instances of hyperthyroidism, many of which were studied both before and after treatment of the condition. Four hundred and ninety-six basal metabolism determinations on 154 patients with hyperthyroidism demonstrated that in all but 16 per cent. the pulse-rate was above 90 per minute if the basal metabolism was +15 per cent. If the basal metabolism fell to normal the pulse-rate reached 90 per minute or below in 78 per cent. Only 5 patients with normal basal metabolism and without hyperthyroidism had a pulse-rate above 90 per minute. There is in general an interrelationship between the pulse-rate and metabolism when a group of individuals are considered: that is, an extreme degree of tachycardia suggests a greatly increased metabolism, while a slight tachycardia usually indicates a slight or moderate increase. The fact that a pulse-rate at complete rest below 90 per minute is seldom and below 80 per minute is rarely associated with an increase in metabolism is of practical importance in the recognition of the large group of nervous patients who have symptoms similar to those occurring in hyperthyroidism.

Observations upon Flutter and Fibrillation.—Part II, III, IV, by LEWIS, FEIL and STROUD (*Heart*, 1920, vii, 191). These papers by the author and his associates represent the results of experiments on dogs' hearts to determine the nature of auricular flutter and fibrillation. Direct graphic registration of the path of the excitation wave in flutter

of the dog's auricle was possible by means of electrodes placed at various points on the auricular wall. The details of the experiments, however, will not be given here. The excitation wave in auricular flutter courses around the orifice of the superior vena cava and surrounds a certain portion of the tissue lying on the inferior caval side of the superior orifice. The movement may be down or up the tenia terminalis. This central wave constitutes a continuous circus movement in a natural ring of muscle existing in the intact heart. "The presence of such a circulatory mechanism would explain long-continued flutter in the human subject and the high rate of auricular beating" and also "the close family resemblance of auricular flutter curves taken from different patients." When slight variations from the general path taken by the excitation wave occur the flutter is impure. "In flutter the excitation wave passes in equal times over equal stretches of auricular tissue; in impure flutter it does not appear to do so, and this is attributed to the establishment of local obstructions or actual barriers (block) which deflect the wave along new and sinuous paths. When this process involves not only the outlying regions of muscle, but also the path of the central wave, it is imagined that auricular fibrillations, as it is spoken of clinically, set in."

Mononuclear Leukocytosis in Reaction to Acute Infections (Infectious Mononucleosis).—SPRUNT and EVANS (*Johns Hopkins Hosp. Bull.*, 1920, xxxi, 410) report on six instances of mononuclear leukocytosis in response to an acute infection whose causal agent is unknown. All the patients were young adults. The symptoms were those of an acute infection associated with large, tender, cervical glands and usually with similar glands in axillæ and groins. The spleen was palpable in four instances. Fever was present for two to three weeks. The blood picture was strikingly similar in all the cases. There was a normal leukocyte count early in the disease followed by a leukocytosis of 13,000 to 20,000 per cubic millimeter. The increase was due chiefly to the presence of large numbers of large lymphocytes often in percentages from 30 to 60. The erythrocytes were normal. The prognosis is good. The authors believe the disease may be looked on as a "tentative" clinical entity. It can be differentiated from leukemia only by the subsequent course.

The Relationship of Smallpox and Alastrim.—COPEMAN (*Proc. Roy. Soc. Med.*, 1920, xiii, 237). The author describes an epidemic of alastrim in the counties in England in the summer of 1919, brought there by the captain of a boat from a Mediterranean port. The incubation period was from twelve to fourteen days. The onset was often abrupt, with headache, prostration, pain in the back and nausea. A chill was infrequent. The fever often was 103° or 104° F. The eruption appeared on the second or third day, followed quickly by disappearance of symptoms. One rachitic infant died. The eruption is characterized by the formation of papules, which soon become vesicular, scattered over the chest, abdomen and extremities, and usually later over the face. It rarely appears on the mucous membranes. The lesions often appear on the palms of the hands and the soles of the feet. They

tend to coalesce. The lesions are not umbilicated nor multilocular, and often do not become pustular. Pitting is uncommon. The differentiation from variola and varicella was often difficult. Vaccination against smallpox did not protect and patients who had recovered from the disease were successfully vaccinated against smallpox. The author describes epidemics of a similar disease in Cambridge (in 1903, 154 cases) and in Trinidad (in 1903, 4000 cases). He states that all these variola-like diseases should be controlled as though they were true variola.

Acute Respiratory Infections at the Boston City Hospital.—Locke, Thomas, O'Hara (*Boston Med. and Surg. Jour.*, 1920, clxxxiii, 480). In this article the authors emphasize the importance of special pneumonia services and give some details of the plan of organization. Some of their statistics are of special interest. Thus in the early weeks of the epidemic of influenza the percentage of cases with pneumonia was low (27 per cent.), but reached 77 per cent. by the ninth week. The epidemic by that time was rapidly subsiding. The death-rate, however, was highest during the early weeks of the epidemic and lowest after the thirteenth week. Practically every death among influenza cases was due to pneumonia. Of the 740 influenza-pneumonias the mortality was 54.7 per cent. The examinations of sputum in influenza-pneumonia demonstrated the extreme rarity of Type I and II infection. As a rule, more than one organism was present, the most frequent combinations being pneumococcus Type IV and B. influenzæ. *Lobar Pneumonia:* There were 447 cases of lobar pneumonia from February 3, 1919, to April 30, 1920, with 25.5 per cent. mortality. Of the total number 116 were Type I, 99 Type IV, 71 Type II and 49 Type III. Serum treatment of Type I cases, if employed before the seventh day, was of value. Empyema followed pneumonia in 66 instances. All were due to the pneumococcus following lobar pneumonia, while in cases of empyema occurring with bronchopneumonia none was caused by this organism. All of the latter except two were caused by streptococci. The mortality of empyema was 22.7 per cent.; 17 per cent. for lobar and 69 per cent. for bronchopneumonia cases.

SURGERY

UNDER THE CHARGE OF

T. TURNER THOMAS, M.D.,

ASSOCIATE PROFESSOR OF APPLIED ANATOMY AND ASSOCIATE IN SURGERY IN THE UNIVERSITY OF PENNSYLVANIA; SURGEON TO THE PHILADELPHIA GENERAL AND NORTHEASTERN HOSPITALS AND ASSISTANT SURGEON TO THE UNIVERSITY HOSPITAL.

The Management of Fractures of the Femur.—Moorhead (*Surg., Gynec. and Obst.*, 1920, xxxi, 288) says that war fractures of the femur were the most difficult to manage, the most likely to cause fatalities,

the most productive of deformity. Early in the war the death-rate from these cases was 80 per cent. The treatment of fracture of the femur starts with first aid designed to place the limb at rest in traction in a Thomas splint, or in traction straps with weights attached. Ambulance surgeons and first aid men should be supplied with Thomas splints. The patient and not the fracture will demand attention in the feeble or diseased. Any method that does not combine reduction with early massage and motion fails to give maximum service. The former idea that deformity and disability are inevitable in femur fractures should be abandoned. Two attempts at reduction should be made before skeletal traction or open reduction is performed. For the non-displaced and reducible group, plaster of Paris (spica or molded) is an efficient form of splintage. In the irreducible group, described skeletal traction by transfixation offers a safe and efficient form of splintage. This fracture entitles the patient to a high grade of surgical care and exacts from the surgeon a degree of diligence and skill at least equal to that necessary in the management of many other major surgical problems. Fractures have been too much slighted by surgeons and for that reason the fracture field is being encroached upon by orthopedists, who by their training are better fitted for the after-care than for the initial care of this acute variety of traumatic surgery. There is a great need for standardization and uniformity in fracture work and in no group is this more necessary than in fractures of the femur.

Etiology, Pathology and Clinical Features of Benign Exostoses.—Eliot (*Ann. Surg.*, 1920, lxxii, 228) says that nutritive disturbances and traumata have long been recognized as important factors in the etiology of exostosis. In the former type the exostosis which is frequently multiple disappears when the nutritive disturbance is corrected. Eliot thinks that subperiosteal hematomas are the starting-points for more or less actively growing exostoses. At times these cannot be differentiated from the classic pointed exostosis, the result of continued or repeated friction. Although as a class benign tumors of bone are of slow growth, the case reported by the author reached a length of two inches in thirteen months, although friction played no part in this unusual development.

The Radical Treatment of X-ray Burns.—Davis (*Ann. Surg.*, 1920, lxxii, 224) says that while some of the *x*-ray burns seen today are only of the first and second degrees, the vast majority under his care have been of the third degree. A peculiarity of the burn is that several weeks or months may elapse before the extent of the damage done becomes apparent. The burned area may be considerably hollowed out, the skin is hairless and atrophied, smooth, dry and shiny, with or without a blotchy brownish pigmentation. In the majority of cases telangiectases are present. The tissue is hard and board-like and its outline may be quite regular. There is usually an irregular shaped patch of tightly adherent necrotic tissue occupying the central portion of the ulcer. They heal slowly, if at all, and then break down. They are exquisitely tender. Davis does not think there is any greater tendency to malignant degeneration in chronic *x*-ray burns than in

any other ulcer, unless the ulceration follows the breaking down of a patch of keratosis. Recent *x*-ray burns of all degrees should be treated as ordinary burns, but unless there is a fairly prompt response to such treatment, it is a mistake to continue it. In third-degree burns the ulcer and surrounding area of induration should be excised with a wide margin, down to healthy tissue. After excision the defect should be grafted immediately if the base of the wound is of normal tissue, but if doubtful tissue is left, grafting should be deferred until granulations form. The type of graft used depends on the situation.

Sarcoma of the Clavicle.—Caley (*Ann. Surg.*, 1920, lxxii, 231) reports 109 collected cases of sarcoma of the clavicle, fifteen of which were under the author's observation. The author thinks that malignant tumors of the clavicle are comparatively rare, only 16 cases having occurred in about 275 cases of sarcoma of the long bones. Sarcoma of the clavicle occurs more frequently in men than in women, probably because of the greater liability of the clavicle to injury in the sex. A clinical history of pain and localized swelling of the clavicle usually following recent injury, with rapid increase in size, supplemented by a fairly characteristic *x*-ray picture, will usually make an early diagnosis comparatively easy without the necessity of an exploratory operation. Local removal of the tumor or even a limited, partial resection should be avoided. The treatment of choice, while the tumor is in an operable stage, should be total excision of the clavicle as soon as the diagnosis is made. As soon as possible after operation, a course of systemic treatment with the mixed toxins of erysipelas and Bacillus prodigiosus should be begun and continued for a period of at least six months. When possible this should be supplemented with local or regional treatment with radium or *x*-rays. The mortality of total excision of the clavicle under modern technic is so small as to be practically disregarded and the functional use of the arm remains unimpaired.

Gall-bladder Disease.—Jacobson (*Arch. Surg.*, 1920, i, 310) gives a statistical study of gall-bladder disease. Next to appendicitis, gall-bladder disease is the commonest intra-abdominal lesion. From 5.7 to 6 per cent. of patients coming to autopsy show gall-stones. Of 80,802 autopsies only 16 per cent. had symptoms referable to gall-stones. W. J. Mayo, in 1244 cases in which operation was performed for uterine myoma, found incidentally 7.2 per cent. of gall-stones, and Peterson, of Ann Arbor, found 12.5 per cent. in 1056 cases with gynecologic lesions. At the Peter Bent Brigham Hospital there have been 470 or 4.1 per cent. of the surgical admissions in six years admitted with a diagnosis of gall-bladder disease. Of these, 397 came to operation. Gall-bladder disease—cholecystitis and cholelithiasis—is a disease of middle age occurring with special frequency in women and closely associated with the increasing incidence of pregnancy. Many cases evidently originate in early age and persist with only vague indefinite symptoms until later in life. Gall-stones are due in all probability to a hematogenous infection, commonly streptococcal, of the gall-bladder and biliary passages and are associated with an

altered cholesterin-content of the blood. Common duct and pancreatic complication are of frequent occurrence in the long-persisting cases. There appears to be no special dilatation of the extrahepatic biliary passages in the slow obliteration of the gall-bladder through chronic infective processes with fibrosis. Recurrences are due mainly to overlooked or reformed stones, persistence of the original infection or to its extension as a chronic pancreatitis. Injury to the biliary passages during operation is due to the rather frequent abnormalities in the bloodvessels and biliary passages. Cholecystectomy is the operation of choice in cholecystitis and cholelithiasis whenever feasible. There is a marked beneficial effect in the long-continued drainage of the biliary passages in the complicated cases of cholecystitis and pancreatitis. There is no special detrimental effect of cholecystectomy on the body economy. There is an increasing mortality rate with the increase in the complications of disease. This is an argument for early diagnosis and operation.

Distribution of Adenomyomas Containing Uterine Mucosa.—CULLEN (*Arch. Surg.*, 1920, i, 215) reports 18 cases in which adenomyomas consisting of a matrix of unstriped muscle and fibrous tissue with typical uterine mucosa scattered throughout were found in the uterus, the rectovaginal septum, the tubes, round ligaments, uteroovarian ligaments, uterosacral ligaments, sigmoid flexure, rectus muscle and umbilicus. Occasionally normal uterine mucosa are found in the ovary. Adenomyomas form one of the most interesting groups of tumors that have to be dealt with in the female pelvis. The cases are reported with complete histories and pathological reports and each case is well illustrated.

Intussusception Resulting from Benign Tumor of the Intestine.—WILLIS (*Surg., Gynec. and Obstet.*, 1920, xxx, 603) says that from the standpoint of the surgeon it is usually held that benign tumors of the small intestine are comparatively unimportant. King, in 1917, was able to find only 118 cases of benign intestinal tumors where the diagnosis was confirmed histologically. In the past ten years Willis has had one case of fibroma and two cases of adenoma of the small intestine. He reports these cases and concludes that the possibility exists that benign tumors of the small intestine are of more frequent occurrence than the number of cases reported from surgical clinics would lead one to suspect. In 4165 autopsies performed at the Boston City Hospital adenomata of the small intestine were encountered four times. We do not often see these tumors in the operating room except when they are the cause of an acute obstruction of the bowel.

Tuberculosis of the Breast.—HAMILTON (*Surg., Gynec. and Obst.*, 1920, xxx, 567) reports a case of tuberculosis of the mammary gland. The patient was forty-four years old. The patient's husband died of tuberculous laryngitis eight years ago. The patient had pulmonary tuberculosis five years ago, the sputum being positive. The history of the present illness was as follows: Injury to the right breast three

weeks before, after which it became tender and sore and a lump appeared. A radical breast operation was performed. In reviewing the literature, Hamilton finds Sir Astley Cooper, in 1829, reported the condition macroscopically, while Dunbar, in 1881, reported microscopic examinations of the breast. Only 180 cases have been reported to date. Deaver and McFarland classify tuberculosis of the breast as primary and secondary. The avenue of entrance of the tubercle bacilli may be through abrasions of the skin of the nipple or from other primary foci. Slight trauma has been the exciting cause in a large percentage of the cases. The prognosis of primary tuberculosis of the breast is good, but in secondary tuberculosis the prognosis depends upon the primary focus.

THERAPEUTICS

UNDER THE CHARGE OF

SAMUEL W. LAMBERT, M.D.,
NEW YORK,

AND

CHARLES C. LIEB, M.D.,
ASSISTANT PROFESSOR OF PHARMACOLOGY, COLUMBIA UNIVERSITY.

The Digestion of the Tannin Compounds Used as Intestinal Astringents by Artificial Digestive Mixtures. Synthetic Drugs, III.—Owing to the too irritant properties of free tannic acid in the stomach, various compounds of tannic acid with proteins, organic esters of tannic acid, etc., have been proposed, which theoretically are presumed to be insoluble in and largely unchanged by gastric juice but to be decomposed by the intestinal secretions. LEECH (*Jour. Am. Med. Assn.*, 1920, lxxv, 1120) studied a number of these preparations to determine: (1) During a specified time the solubility of the respective compounds in water, hydrochloric acid solution, acid and pepsin solution, sodium bicarbonate and pancreatic extract solutions, and (2) the percentage decomposition at various intervals during the digestion. He arrives at the following conclusions: Only one type of the tannic acid compounds studied completely resists the action of the gastric juice and is broken down in the intestine according to theory, *i. e.*, the diacetyl tannic acid compound. "Acetannin Calco" (one specimen only studied) was satisfactory. "Tannigen" was fairly satisfactory in some instances. "Protan" and "Tannoform" were both readily soluble in sodium bicarbonate mediums. They are probably not broken up to a great extent in the intestine. "Albutannin Calco" and "Albutannin M. C. W." were not nearly so resistant to the acid-pepsin digestion as "Tannalbin" and "Tannin Albuminate Exsiccated" (Albutannin Merck). Neither of the two latter was sufficiently

resistant to the acid-pepsin medium but both liberated free tannic acid in the alkaline-pancreatic medium. With the exception of the (single) specimen of Acetannin, none of the products which were examined according to the methods described in this paper conformed strictly to the claims made for them.

The Use of Arsphenamin in Non-syphilitic Diseases.—From a study of the literature, REASONER and NICHOLS (*Jour. Am. Med. Assn.*, 1920, lxxv, 645) conclude that for practical therapeutic purposes the beneficial effects of arsphenamin and neo-arsphenamin are most apparent in a limited number of spirochetal diseases. They act as a specific in Vincent's angina, relapsing fever, yaws, gangosa and pulmonary spirochetosis (if given early) in man, and in equine influenza. A therapeutic effect is noted in rat-bite disease, in certain dental conditions and in fowl spirochetosis. Good results have been obtained in syphilitics with a number of non-syphilitic conditions which are influenced adversely by that disease. Their use has been recommended in conditions in which arsenic is indicated; in such cases the effect is alterative rather than specific and there is no special advantage over liquor potassii arsenitis. No apparent benefit has been found in such other spirochetal diseases as Weil's disease and yellow fever. There is a limited effect on certain protozoal diseases, such as malaria (tertian and quotidian), some of the trypanosomiases and leishmaniasis. This effect may be non-specific. With the exception of anthrax and possibly glanders few favorable results are reported in bacterial diseases. Except in Vincent's angina, arsphenamin and neo-arsphenamin should be administered intravenously in medium-sized dosage. Two or three injections usually are sufficient, except in pulmonary spirochetosis which may require a series of injections. In diseases showing liver involvement, neo-arsphenamin has been recommended, as it is supposed to be less toxic than arsphenamin.

PEDIATRICS

UNDER THE CHARGE OF

THOMPSON S. WESTCOTT, M.D., AND ALVIN E. SIEGEL, M.D.,
OF PHILADELPHIA.

Further Progress in the Study of the Relative Efficiency of the Different Mercurial Preparations.—RAMSEY and GROEBNER (*Am. Jour. Dis. Children*, September, 1920) found that mercurial ointment, 50 per cent., is to be preferred to the less concentrated forms and need not be repeated more often than twice a week instead of daily. The quantity of mercury absorbed is much increased by friction. Calomel ointment is absorbed but less rapidly, and to a less extent than the mercurial preparation, and should, therefore, be given in greater concentration. The salicylate of mercury in oil should be given hypoder-

mically twice a week instead of once a week. Mercuric chloride, by hypodermic injection, although the dose is very small, continues to be eliminated for six or seven days. The fact that its use is frequently followed by the appearance of protein in the urine should exclude it from the treatment of syphilis in children. Calomel by mouth is absorbed in small amounts and continues to be eliminated for a considerable time, so that it would be sufficient to give it at intervals of several days, in order to avoid diarrhea. Gray powder is absorbed to a small degree and eliminated rather rapidly, so that large doses repeated daily would probably be needed to maintain mercury in the circulation.

A Study of Streptococci Obtained from the Mouth in Cases of Chorea.—Floyd (*Jour. Med. Research*, May, 1920) reports as a result of experimental work in the production of endocarditis, acute articular rheumatism and chorea one or more members of the group of streptococci have been found to be the organisms producing pathologic results. Positive cultural results in clinical cases have mainly shown the streptococcus group. The clinical sequence of tonsillitis, articular rheumatism, with chorea or endocarditis, points to a localized lesion producing periodic systemic infection. Experimental work shows a much higher percentage of carriers of certain types of virulent streptococci in the substance of the tonsils and about the teeth in cases of chorea than occur in normal controls. The frequency with which virulent strains of streptococci are found in the mouth in cases of infection of the meninges, the joint surfaces and the endocardium suggests more than a casual relationship between their presence in the mouth, and systemic disease. He suggests that the teeth and tonsils are in all probability the two portals of entry into the body for streptococci in producing any of these clinically grouped diseases.

Spasmophilia and Vitamins.—Von Meysenburg (*Am. Jour. Dis. Children*, September, 1920) thought that in view of the similarity between beriberi in its early stages and active tetany, a deficiency in the diet of the antineuritic vitamine might play a role in the causation of spasmophilia. In both conditions the nervous system is involved, giving rise to such symptoms as hoarseness and laryngospasm. The end-results of the two conditions are, however, entirely different, beriberi being rapidly fatal if not treated and spasmophilia terminating in death. The studies of the author served only to rule out any possible relation between the heightened electrical irritability or the so-called spasmophilic reaction and any deficiency in the diet of the water-soluble vitamin. The infants studied in this group all received liberal allowances of orange-juice in their dietary, yet they showed the electric reactions characteristic of spasmophilia. This was all the more interesting because of the antineuritic content of orange-juice as shown by Osborne and Mendel and later by Byfield and Daniels. The very frequent association of spasmophilia and rickets, and the prominence which has been given to the fat-soluble vitamines in connection with rickets, serves only to add interest to the normal electric reactions obtained in those children whose diet contained a minimal quantity of this factor. The evidence of these cases shows that increased electric reaction is not dependent on a deficiency in the diet of the water-soluble vitamine or of the other two known food accessory factors.

Three Pertinent Questions on Maternal Feeding.—Mulherin (*Jour. Am. Med. Assn.*, September 25, 1920), in answer to the query as to the advisability of immediate weaning in uncomplicated pregnancy, says that Nature does not intend the mother to nurse a baby at the breast and to furnish nourishment for one in the womb as well. He states that pregnancy itself does not generate toxins or cause them to be formed in the mother. It is the exception rather than the rule for toxemia to complicate pregnancy. It is true, however, that pregnancy as a rule, causes a diminution in the flow of the milk, and the quality is lowered especially of the fats. Because of the difficulty of changing directly from maternal feeding to cow's milk, both in the mother pregnant with another child and in the mother suffering from typhoid fever, he advocates complemental feeding. By complemental feeding he means an artificial feeding given the baby after it has nursed. This differs from supplemental feeding, which is an artificial feeding in place of a breast-feeding. In order to successfully practice complemental feeding a few points must be remembered: After the baby has nursed from the breasts they must be emptied by manual manipulation of finger-milking. In cases where the baby is too weak to suckle the milk must be expressed from the breast and fed by means of a spoon or dropper. He claims that supplemental feeding is wrong in both principle and practice, but that with complemental feeding, breast-feeding can be established, maintained and reinstituted.

The Superior Longitudinal Route.—McKee (*Therap. Gaz.*, September, 1920) points out that in the study of infantile disease blood is frequently needed for cultural or biochemic studies. In the past it was difficult to procure. Intravenous therapy in infants as in adults is coming more and more prominently into use. Because of the small superficial vessels in infants it has been difficult to follow this method. The superior longitudinal sinus is a relatively large vessel, very near the surface of the body. Its walls are resistant, it is not easily displaced and it does not occupy anomalous positions. It would seem, therefore, to be the ideal to enter when blood is needed for laboratory investigation or when intravenous medication is required. There is little danger in entering the vessel, but no one should puncture a baby's fontanelle without a due sense of responsibility and without a knowledge of the method and of surgical cleanliness. The scalp should be shaved, scrubbed and painted with iodin. All instruments must be sterilized and the operator should wear rubber gloves. Two assistants are needed, one to hold the head steady and slightly flexed and the other to manage the syringe, tube or transfusion apparatus. The Heimholz needle-holder holds the needle in position and at an angle of 25 degrees. The needle used is a No. 18 or 20 Brown-Smith.

Social and Medical Aspects of Childhood Delinquency.—Brown (*Jour. Am. Med. Assn.*, October 9, 1920) examined 150 delinquent children of New York and found about one-third could be classified as nervous. They showed various symptoms of either mild or severe character constituting a neurosis. In drawing general conclusions from this survey a few of the most striking features must be indicated. From

a careful observation of delinquent children one cannot but feel that by proper management these conduct disorders might to a great extent be avoided. Usually the child has been misunderstood. Efforts are made to force the child to do something that he is entirely incapable of doing. He may be nervous, lack emotional control or intellectual ability to carry out the task. This is the material from which delinquents are made. Delinquency is often a minor affair at first, but under repeated maladjustments, undesirable habits are developed. Preventive treatment is the only way to manage childhood delinquency. Economic provisions aiming at preventive treatment of these children would not be difficult. Provision should be made for the prompt examination of all cases showing evidence of not getting along well. Special classes in school, and even special schools with vocational classes, would be better than truant schools. Small beginnings have already been made in certain places to accomplish this purpose.

A Note on Vitamines in Relation to Scurvy and Rickets.—Davidson (*Med. Officer*, September 25, 1920) became medical superintendent of a county infant welfare center in 1917. At that time the scarcity of butter and milk was pronounced and mothers and infants showed signs of fat deficiency and insufficient food. Scurvy and rickets were seen in many babies. Those who were not breast-fed were being fed on condensed milk and patent foods. Realizing that this procedure would lead to more rickets and scurvy, the use of all condensed milk and patent foods was condemned. The following method was instituted: All bottle-fed infants were placed on a ration of dried milk plus fruit juice. They all improved up to two or three months, at which period they seemed to stand still. Evidently they lacked something in the diet necessary for growth. Dried milk procured from cows grazed in rough and rocky soil of the hilly country was substituted for that produced from milk of cows pastured in the fertile meadows of the lowlands, because the former was richer in fats and possibly in vitamines. The change was a marked success as the infants increased in weight and became more healthy in appearance. In addition to this red bone-marrow extracted from the rib bones of calves with the addition of a small amount of malt sugar was given. In addition to these things the children received a teaspoonful or two of orange, turnip or lemon-juice.

The Diagnosis and Treatment of Hydrocephalus Resulting from Stricture of the Aqueduct of Sylvius.—Dandy (*Surg., Gynec. and Obst.*, October, 1920) says that cicatricial stenosis of the aqueduct of Sylvius is the most frequent lesion in congenital hydrocephalus, occurring in about 50 per cent. of the cases, and it is also found in a large percentage of cases of hydrocephalus occurring in infancy and early childhood. It may occur, but rarely does so, in adult life. Hydrocephalus always follows occlusion of the aqueduct of Sylvius. The third and both lateral ventricles progressively dilate. The fourth ventricle, being posterior to the obstruction, does not enlarge. In the gross the occluded aqueduct appears to be replaced by a fibrous tissue band, which microscopically is neuroglia. Microscopic remnants of the aqueduct are usually but

not always found. The stenosis may occupy the entire length of the aqueduct or varying parts. It may even be only a thin transparent membrane. The stricture may be only partial. Strictures of the aqueduct can be diagnosed and accurately localized. The indigo-carmin test will indicate that a stricture is present. By ventriculography the obstruction can be definitely located. Spontaneous relief is not possible. Surgical attempts to drain the fluid from the third ventricle to the exterior of the brain have all proved futile. The openings invariably close and the fluid cannot absorb in the subdural space. He suggests a surgical procedure directed to the cause. A new aqueduct is constructed and a tube is left in place for two or three weeks. This has been done on two cases, both recovering from the operation. One died of pneumonia several weeks later, but the other seems well one year after the operation.

OBSTETRICS

UNDER THE CHARGE OF

EDWARD P. DAVIS, A.M., M.D.,
PROFESSOR OF OBSTETRICS IN THE JEFFERSON MEDICAL COLLEGE, PHILADELPHIA.

Treatment of the Severe Vomiting of Early Pregnancy.—Lynch (*Jour. Am. Med. Assn.*, August 16, 1919) contributed a paper upon this subject at the meeting of the American Medical Association. He has examined the statistics of various countries to determine the frequency of this condition. Statistics seem to indicate that the severe vomiting of early pregnancy was less frequent in Germany than in America, England, France and Russia. In the writer's experience 58 per cent. of his private patients gave a history of nausea and vomiting in early pregnancy in 45 per cent. of his hospital cases. So far as serious cases are concerned, Carl Brown is credited with the statement that in 150,000 pregnancies he saw no fatal case. Similar statements were made by other German and Austrian obstetricians. The records of death from pernicious vomiting in France and England indicate a higher mortality. In 1914 Bondy reported only 21 cases of pernicious vomiting in 10,000 pregnancies in Breslau. He quotes similar statistics in two German clinics. In 2750 clinic cases at the University of California Hospital 14 were admitted for the treatment of pernicious vomiting of early pregnancy. The writer believes that in some way in these cases the maternal organism is sensitized to vomiting while in a state of pregnancy. He does not explain what is meant by this statement, nor does he mention the absorption of syncytium, which to many obstetricians is a rational explanation of this condition. Possibly these two causes may be related and frequently appear in common. In the pathology of the condition the changes in the liver are clearly recognized. Milder cases dying of some other condition show little more than the cloudy swelling of the parenchyma of the liver. All fatal cases, or nearly all fatal cases, show decided structural change varying from simple fatty

degeneration to acute yellow atrophy. In the most marked type there are degenerative changes about the central vein of the lobule tending toward its periphery. Clinically these cases have been divided into reflex, neurotic or toxemic. But the clinical classification should depend upon the pathology, and this would indicate that severe cases are toxic and that the toxemia gives its most evident manifestation in changes in the liver. The writer believes that it is problematic whether the pathological picture presented in the liver of those who die from serious vomiting of pregnancy represents the various stages of the same disease. While the writer believes that American obstetricians do wisely in promptly terminating pregnancy when medicinal treatment fails, yet he does not share the opinion of Tarnier and Boudin that the disease does not tend to recur in subsequent pregnancies. He has observed numerous cases in which after the first toxemia of pregnancy others have been complicated in the same way. Recognizing the importance of ammonia in the urine as indicating a pathological condition, the writer believes that this is influenced profoundly by the type of diet and by medication and by other factors. He does not consider ammonia as probably an index of the functions of the liver, but states that the fact remains that it is increased in the condition of acidosis and serves the purpose of saving alkali for the body. His observations have shown him that in more serious cases there is an increase in urinary ammonia. He believes it better to state that ammonia nitrogen in terms of absolute amounts, since without this control the ammonia coëfficient may be misleading. The coëfficient is a proportion of the total urinary nitrogen that presents as ammonia. If the absolute amount of ammonia remains stationary the coëfficient will decrease with the increase of total nitrogen and will increase with the fall of total nitrogen. This has been shown by Folin in studying the variations seen in health. If the total nitrogen remains stationary and the ammonia increases in amount the ammonia coëfficient increases, thus resembling the curve of increase of ammonia by weight. This condition he states is infrequently seen in the severe types of vomiting. These patients are put upon restricted diet and so the total nitrogen in the urine comes largely from the breaking down of body tissues. Early in starvation the loss of weight depends greatly upon loss of fats as the fatty acids are oxidized largely by the glycogen stored in the liver. It is natural to find variations in the partitions of the urinary nitrogen in fat and thin subjects dependent in turn upon the relative importance of carbohydrates stored in the body suitable for oxygenization of the resulting fatty acids. Undoubtedly the character of the food last taken may influence the condition. The writer has studied the acid of the blood in normal pregnancy and finds that there commonly exists in normal pregnancy an acidosis shown by the tension of the carbon dioxide of the blood, although the blood readings in the majority of his vomiting series fall within the same range as cases considered clinically as normal. In studying the urinary ammonia in early pregnancy the writer states that he has never seen a patient, as judged by clinical means, in danger of life in whose urine ammonia was in normal limits. The fact that high ammonia is occasionally seen in cases that do not give symptoms of marked toxicity does not impair the truth of the general statement, since the loss of fatty tissues, the glycogen content of the liver and

muscles, the character of the food retained, the type of medication employed all constitute factors that must be considered in a given case. It has been suggested that this increased ammonia is caused merely by the acidosis of starvation. While it is evident that cases of pernicious vomiting are starving, one cannot believe that starvation is responsible for the entire condition. The variations in anemia seen in pernicious vomiting of early pregnancy greatly exceed those found in cases of starvation. A starving patient after taking food has the ammonia fall very rapidly, and individuals subjected to experimental starvation are able to be up and about. On the contrary, patients in early pregnancy with pernicious nausea have been in bed for some time, and some of them have retained some food by mouth and have received glucose by the blood or by the rectum. The total nitrogen in a woman with the pernicious nausea of gestation often falls below that encountered in any case of starvation. We must admit the existence of acidosis in pregnancy, but the tension of the carbon dioxide in the blood in the cases of pernicious nausea does not exceed that of normal cases in which there is no pernicious nausea. The writer believes that the decision lies in the clinical behavior of the patient. After abortion the conditions often return to normal with the cure of the vomiting, while many others succeed in bringing about this result by proper treatment with the preservation of pregnancy. In the simple cases there is usually an excess of acid in the stomach. Patients are relieved temporarily by taking food and the mouth is acid when tested by litmus. Constipation is almost invariably present. The writer recognizes three periods in the day in which vomiting is liable to occur: (1) in the early morning; (2) late in the afternoon; (3) shortly before noon. Many patients show vomiting in all three. Motor neuroses are very common in these cases. The patient is usually worse in the morning because of the long fast during the night, although the stomach usually empties itself in a normal manner during the night, so that the matter vomited in the morning is chiefly acid mucus. Vomiting may also occur immediately after taking food. The nausea in the late afternoon very commonly follows a bad luncheon, while those patients whose usual breakfast is coffee and rolls often have a wave of nausea about 11 in the morning. Some of the most obstinate cases, however, occur in those in whom the acidity is less than normal. In the management of these cases the writer urges a careful study of the gastric secretions and of all matter ejected. He believes in the importance of nervous reflexes, and posterior displacements of the uterus should be corrected and the uterus held in normal position by pessaries, although the writer states that he has never seen relief follow such treatment alone. The care of the bowels is exceedingly important and may be a matter of much difficulty. But few drugs should be used. Rest, ventilation, hygiene and proper clothing are all important. That vomiting may be a nervous habit entirely is the belief of the writer. Hence the importance of trying to break the habit by selecting the type of food most easy to digest and difficult to vomit. Absolute rest and quiet are of the greatest importance. Hospital care is best and patients are usually relieved in about ten days. The writer's cases are put to bed and food and drink by mouth stopped until there has been no vomiting for twenty-four hours; the bowels are kept open by Bailey high colonic flushing; 40 to 60 grains of bromide are given by the bowel every four hours; 8 to 10 ounces of glucose and

soda are given by the rectum at fixed intervals. The patient should be assured that when the first meal is given she will be able to retain it, and she is strongly urged not to form the habit of vomiting. In selecting food fruits or sweets are to be avoided. The meal should be of solid food. While there is excess of acid a diet of proteins, limited fats and restricted carbohydrates is best. A deficiency of carbohydrates is supplied by the glucose given by the bowel, while the sodium bicarbonate neutralizes the acidosis. A diet of meats, fresh toasted bread and butter, a small amount of milk and cream is especially useful. Four meals of such food should be taken in twenty-four hours. Fluid may be withheld by mouth for many days and until the diet has been extended to include vegetables. Then the meals may be solid and fluid in alternation in small quantities and at frequent intervals. Usually broiled steak, roast beef and slightly cooked scraped beef are best, and must be used for several days. If this can be done the diet may be enlarged. When the case is of the subacid type it is more difficult to manage and the diet must be enlarged and fewer meats used. As the patient improves the bromides are reduced and soda and magnesia are given in capsules by mouth during digestion. The writer has found ingluvin of value in some cases. The writer is strongly convinced that food should be solid, frequent and in small quantities. Liquid foods he believes are very easily vomited. He believes that patients crave acid drinks, but that this craving can often be satisfied by a mouth wash containing acid. It is difficult to manage these patients without good nursing, and the nurse must strictly follow the physician's orders. If the case is of a fulminating type or if black vomit occurs pregnancy should be interrupted at once. Very often it is too late when these symptoms manifest themselves. The writer states that we do not know a safe limit for the urinary ammonia. There is a close parallel, he believes, between the ammonia excretion of pernicious nausea of pregnancy and that seen in diabetes. He has used Ringer's solution with excellent results, given alternately with the glucose-soda solution. He has tried injections of normal pregnant serum, but without result. Corpus luteum and epinephrin have been of no value. If the acidosis is not influenced by treatment and symptoms continue severe abortion is indicated. When marked acidosis is absent the prognosis is more favorable. In making the prognosis the study of the urinary ammonia is of value. The newer methods of Folin and Van Slyke can be carried out by hospital interns and titrations with formaldehyde solution are sufficiently accurate for clinical purposes and comparatively easy to carry out. The method of abortion is important because the anesthesia sometimes creates great danger. Chloroform should never be used in any case in which it would appear that the liver has used up most of its glycogen. Chloroform causes serious damage to the liver, already the seat of a pathological process. Ether produces acidosis and adds to the vomiting. Anesthesia with nitrous oxide and oxygen enough given to complete anesthesia are indicated. If the fetus cannot be removed with the dilatation obtained by the solid dilator, vaginal hysterotomy may be indicated, especially if the cervix is long and high. The lessened resistance of the patient to infection must not be forgotten. The use of bags and packing often aggravate the symptoms. The bladder should not be invaded if infection and pyelitis are readily developed.

GYNECOLOGY

UNDER THE CHARGE OF

JOHN G. CLARK, M.D.,

PROFESSOR OF GYNECOLOGY IN THE UNIVERSITY OF PENNSYLVANIA, PHILADELPHIA,

AND

FRANK B. BLOCK, M.D.,

ASSISTANT INSTRUCTOR IN GYNECOLOGY, MEDICAL SCHOOL, UNIVERSITY OF PENNSYLVANIA, PHILADELPHIA.

Conservatism in Pelvic Inflammatory Disease.—Based upon an experience with 120 patients upon whom he has performed wedge excision of the fundus uteri in the treatment of inflammatory disease, SCHMID (*Arch. f. Gyn.*, 1920, cxiii, 164) summarizes his views upon the treatment of pelvic inflammatory disease as carried out in the gynecologic clinic at Prag. In the acute stage, the cases are treated conservatively in order that the diffuse peritonitis may have a chance to localize and possibly completely disappear. In the chronic stage, simple conservative measures will, in three-fourths of the cases bring about complete restoration or at least sufficient improvement so that the patient may resume her usual occupation. Minor operations on the adnexa can then be performed, such as release of adhesions, removal of one tube or the adnexa of one side followed by salpingostomy on the other side if the remaining tube is healthy or shows only minor changes. In severe disease of both sides in which the retention of one ovary is precluded, and in women over forty years with moderate bilateral disease, a radical operation should be done by the abdominal route. In cases of bilateral inflammatory disease in which at least one ovary can be conserved, if the patient is in the child-bearing age, both tubes and the more seriously diseased ovary together with a wedge-shaped portion of the fundus uteri should be removed while the less diseased ovary or at least a portion of it should be allowed to remain. This fundus excision, which has recently been advocated in this country by Polak and known as the Bell-Beuttner operation, gives no higher mortality than the more conservative operations and has a lower mortality than the radical vaginal or abdominal operations. With proper technic it gives a subjective as well as objective satisfactory end-result in 83 per cent. of the cases with freedom from menopausal symptoms as well as the psychic shock of amenorrhea and with relief from pain and a complete restoration of the patient to her usual occupation.

Differential Diagnosis of Tumors by Means of Roentgen Ray.—By showing the manner in which neoplasms react to roentgen radiation, SEITZ and WINTZ (*Münch. Med. Wchnschr.*, 1920, lxvii, 653) believe that they have found a means of differentiating benign from malignant tumors. After roentgen radiation, if the tumor begins to show regression in a few days and has more or less completely disappeared after four or five weeks, it is probably a sarcoma. If, on the other hand, the regression

of the tumor after radiation first appears after three or four months and continues very slowly, consuming one to two years for complete disappearance, it is a myoma in all probability. The diminution in the size of the myoma is a secondary effect and is due to ovarian influence. The young cells of malignant tumors are much more sensitive to the roentgen rays than are the mature cells of benign neoplasms and thus roentgen-ray treatment often assists in making a differential diagnosis between benign and malignant tumors. For example, a lymphosarcoma regresses very quickly under radiation, while a tuberculous glandular swelling disappears very slowly. Similarly in the differential diagnosis between carcinoma and sarcoma the roentgen ray may be of assistance. Large ovarian and abdominal sarcomata regress quickly after radiation while carcinoma reacts very slowly unless a carcinoma dosage is given, which of course is much larger than the ordinary dosage.

Operation for Pruritus of Anus and Vulva.—The operative treatment proposed by ALLEN (*New Orleans Med. and Surg. Jour.*, 1920, lxxiii, 127) has in view the separation of the skin from the underlying tissue thus dividing all the nerves which reach the affected parts, rendering them anesthetic, and preventing the skin from immediately healing to the underlying tissues by packing, which is kept up until a firm bed of granulation has formed, which usually requires about one week, when the packing is discontinued and the skin allowed to fall back in place where it soon is again firmly united, leaving an anesthetic area which nearly equals the extent of the undermined area. This anesthetic area is not complained of but is usually a quite welcome change. It gradually diminishes in size with the return of normal sensation after a few months and has in Allen's experience not been followed by a return of the pruritus. The operation upon the anal region is the simpler. The area involved must first be accurately determined. It is usually quite symmetrical and uniform on both sides. A series of incisions are now made beginning at the anal margin and continued outward to about one-half inch beyond the affected area, which is rarely more than two inches. A series of these incisions are made about one inch apart at the peripheral extremity until the entire perineal region has been covered. These skin strips are now dissected up, preferably with a scalpel, except at their two ends which are left attached. In separating the skin from the subcutaneous tissues but a small margin of tissue is left attached to its under surface to insure a sufficient circulation to prevent sloughing. As the pruritic area rarely involves the mucous surfaces the incisions need not invade them, and in a few cases where the vaginal mucosa seemed to have been involved it cleared up with the relief of the external parts. The operation upon the vaginal outlet is performed in the same general way as upon the anal region and should need no special description. After dissecting up the skin flaps the space beneath is packed with iodoform gauze. Frequent sitz baths with a liberal supply of soap has always been insisted upon as an after-treatment. They keep the parts cleansed and are more effective and comfortable than irrigations. The packs may occasionally need changing but often remain the full time, about one week. After the packs are removed the parts quickly unite. The total disability is about two weeks.

Treatment of Inoperable Cancer with Selenium.—The attempt to eradicate malignant disease by injection into the blood stream is of recent origin. The pathogenesis of cancer is as yet unknown, but it has long been our hope to discover some preparation that would cause the destruction of the proliferating cells, whether this proliferation be the entire morbid process or merely the manifest termination of other hypothetical local changes. It having been observed, however, that cancerous tissue possesses the property of concentrating in itself the mercury given for the treatment of syphilis, experiments have been conducted to discover if other elements might not likewise be selected with this object in view; for it appeared possible that, if it were so, a protoplasmic poison might be given in doses which, though small enough not to injure the patient, might yet become sufficiently concentrated in the cancerous cells to effect their destruction. It was found that a large number of elements, chiefly metals and metalloids, showed this affinity in greater or less degree. WATSON–WILLIAMS (*British Jour. Surg.*, 1920, viii, 50) has been working along these lines with selenium. He states that the treatment appears to be suitable for two classes of patients. In inoperable cases, the results obtained compare favorably with any known method of attacking the growth by the blood stream, and are approximately equal to those of radiotherapy. The moderate focal reaction is in no way comparable to the local reaction from radium: the preparation appears to be considerably more active than copper. All malignant tissue is affected, however inaccessible. As a purely palliative treatment, the drying of ulcers and abolition of pain is a marked advantage. The injections have the minor advantage of low cost. As an adjunct to operative measures, including diathermy, the treatment may be applied to a variety of conditions. Where operative removal has not been as free as desirable, the possible outlying cells might be destroyed by injections. In patients having a course of injections, wounds in carcinomatous tissue have been observed to heal. Cases pronounced inoperable may give hope of becoming operable when sepsis and fixation have been diminished by this treatment. Possibly malignant processes might be held in check for a few weeks in patients who cannot arrange to submit to an operation at short notice: time is necessary before deciding as to the value of selenium in such cases. The effects following a course of injections are usually well marked. They are gradual in their appearance, and the improvement continues for some time after the injections have ceased. The first effect is noticed by the patient and is a local one, namely, diminution or disappearance of pain. In a favorable case there follows diminution in tenderness, cleansing of ulcerated surfaces, decrease of discharge, granulation, diminution in size and hardness of the tumor and secondary deposits, increased mobility of the part. In the general condition one may note improvement in anemia and cachexia, improved sleep and memory, increase in weight and strength, marked psychic improvement: this is due partly, no doubt, to the feeling that something is being done but is also largely attributable to relief from pain, sleeplessness and the intolerable discomfort of fetid discharges.

Combined X-ray and Radium Treatment of Uterine Carcinoma.—It has been the practise of SKINNER (*Amer. Jour. Roentgenology*, 1920, vii, 376) to accept no case for postoperative radiotherapy of a pelvic lesion unless deep *x*-ray intensive exposures through multiple portals of entry were used in an attempt to control the lymphatic metastasis at the same time that radium was applied to the cervix or uterus He believes that the results obtained by roentgen therapy alone, before radium came into general use, warrant its continuation. By observation, he has acquired a criterion of prognosis in these cases, which is that cases which exhibit an early tanning of the skin offer the best prognosis. It is realized that tanning is a matter of skin type to a certain extent, and that it could be a matter of dosage and filtration. But when a uniform technic is used daily, he has constantly noted that the cases which tan quickly are doing better than those which do not tan. He is convinced that this is worthy of observation, as variation in technic did not produce tanning in the case that was losing the fight. It is generally acknowledged that the limits of radium activity producing reduction of cancer cells is 2 to 3 cm. which means that radium can have no action upon the pelvic lymphatics and other channels of metastatic progress unless there is an open operation which permits the planting of radium directly to the suspicious tissues or unless a large amount of radium is available to reproduce the effects of cross-fire roentgenization of these tissues. On the other hand, the limits of roentgen therapy are not measured by 2 or 3 cm., and the ability to cross-fire and thus accumulate *x*-ray tissue effects at any depth is simply a matter of careful and tedious technic. The question of the vulnerability of neoplastic tissue has been followed up in clinical and physiological observation. The cells are destroyed more readily in their lower state of development than in their more adult state. The aim of the postoperative radiations is not merely to destroy any cells which may have been left, but to prevent in the earliest stages the development of recurrences, and with this idea in mind the irradiations should be continued for a length of time at increasing intervals, sufficient to cover the period of probable recurrence.

PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

OSKAR KLOTZ, M.D., C.M.,

PROFESSOR OF PATHOLOGY AND BACTERIOLOGY, UNIVERSITY OF PITTSBURGH, PITTSBURGH, PA.

The Action of Benzol.—WEISKOTTEN, GIBBS, BOGGS and TEMPLETON (*Jour. Med. Res.*, 1920, xii, 425) report an interesting series of rabbit experiments on the action of benzol. The suggestion for this work was provided by the report of Selling (1910) of a series of cases of benzol poisoning occurring in girls in a factory where the rubber for soldering was held in solution in benzol. The predominating clinical features in these instances were purpura hemorrhagica, anemia and leukopenia.

Later in animal experimentation, Selling, and White and Gammon were unsuccessful in many attempts to produce anemia and leukopenia in well rabbits by the inhalation method *per se*, although Selling was able to obtain the desired result by the hypodermic injection of benzol in olive oil. In the present series, healthy rabbits were placed in a chamber containing vaporized benzol in concentrations comparable to that occurring in the factories. No accurate check on the amount of benzol was made although it was endeavored to maintain a maximal sublethal dosage. The average amount of benzol vaporized was 16.6 c.c. per hour. By meter it was found that 71.4 liters of air-benzol mixture were being pumped into the animal chamber every hour. Eleven animals were used. Six of the rabbits were placed in the chamber for ten hours daily while the remaining five were constantly immersed in benzol vapor excepting for a few minutes each morning when they were removed for purposes of weighing and blood analysis. The results were similar in both sets of animals. Within the chamber maximal sublethal dosage of the vaporized benzol was persisted in until the animals ceased to eat and were quite ill, at which time, if exposure was not complete, the concentration of the benzol vapor was diminished sufficiently to permit the recovery of the rabbits. Of the eleven animals only four survived the tests and autopsies performed upon the dead rabbits showed edema of the lungs, pulmonary and gastro-intestinal hemorrhages and ulcerations of the gastric mucosa to be the outstanding features. It is noted that in the leukocyte curves and erythrocyte curves, a permanent lower level was struck following the subjection of the rabbits to the benzol vapor. In the case of the leukocytes this was reached about the sixth day after exposure while in that of the erythrocytes it was attained from the sixth to the sixteenth days. All animals demonstrated a definite weight loss which continued throughout the period of exposure. The authors through their careful investigations, demonstrated conclusively that exposure of rabbits to benzol vapor with maximal sublethal dosage causes leukopenia, hemorrhages, weight loss and anemia, and that in the leukopenia the percentage and absolute decrease is greater in the small mononuclear cells than in the polynuclear amphophiles. It is observed, in addition, that after the discontinuance of exposure to benzol vapor the leukocyte curve gradually rises to a permanent general level which however, is much lower than the normal permanent level prior to exposure and that the failure to return to normal is due to the inability of the small mononuclear curve to return to its preëxisting state.

Effect of Intrabronchial Insufflation of Acid.—The resemblance between the lesions of influenzal pneumonia and those produced by the inhalation of irritating gases suggested to WINTERNITZ, SMITH and MCNAMARA (*Jour. Exper. Med.*, 1920, xxxii, 199) a series of experiments which might assist in the interpretation of the characteristic influenzal lesions. Inasmuch as the weight of evidence indicates that the lesions which these gases produce depend on the halogen radical and that the decomposition of these gases is associated with the formation of hydrochloric acid, this reagent was introduced by intrabronchial insufflation into rabbits in dilutions varying from 0.1 to 1.0 per cent. dilution. It was found that the acid so administered caused an immediate and

extreme damage of lung tissue. Within certain limits the degree and extent of injury varied according to the concentration of the acid. With greater concentrations death occurred almost immediately, while with weaker solutions the results, grossly and histologically, resembled those noted after influenzal pneumonia and gas poisoning, being associated with intense edema and congestion of the lung with hemorrhage, dilatation of the alveolar ducts and bronchioles, hyaline necrosis of the epithelium of these structures, and lobular, pseudolobular, and lobar types of consolidation which were mostly serofibrinous but sometimes hemorrhagic or purulent.

Histological Changes of the Different Types of Carcinoma after Exposure to Radium Rays.—ALTER (*Jour. Med. Res.*, 1920, xli, 439) presents a review of comparative studies of the effect of radiation upon the various carcinomata and incidentally gives an estimation of the worth and the limitation of radium in the clinical field. Broadly, the writer groups the malignant tumors into a combined histological and anatomical classification and by microscopical description demonstrates the variations in reaction to radium by the different types of growth. Beginning with the basal cells, cancers of skin, the less specialized and most embryonal types, wherein radium produces a complete destruction and absorption of the tumor cells, the author gradually ascends the scale to the tumors derived from highly specialized, particularly functioning epithelium in which the radiation results in the extreme opposite, namely that of hastened functional activity or specialization. However, it is not inferred that the process in the latter series is uninterrupted for here, too, much of the undifferentiated tissue succumbs and is absorbed. Apparently each type of carcinoma has a particular mode of response to radiation and this reaction is determined to a great degree by the physiologic function or grade of specialization of the particular type of cell in the body. So it is that the embryonal basal cell tumor with no especially differentiated characters "melts away" before radium, while just a step higher the prickle cell cancer though partially destroyed, is hastened toward its particular form of differentiation. The adenocarcinomata tend to approach the normal character of the tissue and manifest hypertrophied function under the stimulus of radiation. The inference is clearly drawn that the least differentiated types of tumors are more prone to destruction by radium and therefore this mode of treatment has its maximum value in such cases. The author states that all tumors undergo a period of latency following radiation subsequent to which a primary swelling of the cells occurs. From this point, in the basal cell types, a progressive destructive process ensues, while in the differentiated types the specialized functional activities are hastened. It is clearly shown that the response to radiation is no more than an expression of transformation of energy. The energy required in the fulfilment of the hastened functional activities can be derived only at the expense of one other source, namely, from the capacity for multiplication and growth. This is corroborated by the infrequent finding of mitotic figures in the nuclei of cells subjected to radium therapy. Hence the retardation in growth of tumors following radiation is easily explained. The degree of effect of radium rays on tumor

cells, the author maintains, is proportionate to the amount of rays absorbed and that different nuclei and protoplasm absorb different amounts. The quantity absorbed is dependent upon intracellular physicochemical or chemical conditions which the writer feels would furnish an interesting field for study.

HYGIENE AND PUBLIC HEALTH

UNDER THE CHARGE OF

MILTON J. ROSENAU, M.D.,

PROFESSOR OF PREVENTIVE MEDICINE AND HYGIENE, HARVARD MEDICAL SCHOOL, BOSTON, MASSACHUSETTS,

AND

GEORGE W. McCOY, M.D.,

DIRECTOR OF HYGIENIC LABORATORY, UNITED STATES PUBLIC HEALTH SERVICE, WASHINGTON, D. C.

Notes on Typhus.—WOLBACH, TODD and PALFREY (*Internat. Jour. Public Health*, September, 1920, No. 2, i) were members of the Typhus Research Commission of the League of Red Cross Societies to Poland. They did their work last winter in Warsaw. These investigators planned a series of experiments with the purpose of determining the nature and specificity of microörganisms acquired by lice fed on typhus fever patients. Thirteen unsuccessful attempts were made to cultivate the organism described by Plotz. They find that the distinctive pathology of typhus fever is microscopic. The disease is characterized by lesions in the smaller bloodvessels. The vessels of the skin and the smaller vessels of the central nervous system are most often affected. The earliest lesion noted is a reaction of the endothelium, which proliferates, followed by degeneration and necrosis. In larger vessels these processes lead to a formation of thrombi; in smaller vessels there is sometimes a destruction of continuity followed by an extravasation of blood. This occurs most often in the capillaries of the skin and brain. Occluding thrombi of the larger arteries and veins of the skin frequently occur, but mural thrombi are constant. These changes are so characteristic that a diagnosis of typhus fever can be made from the skin excised during life; in only one other disease, Rocky Mountain spotted fever, do similar lesions occur. In the endothelial cells of vessels presenting lesions a microörganism has been found. This is similar in appearance to that described in Rocky Mountain spotted fever (Wolbach: *Jour. Med. Res.*, November, 1919, p. 197) and in the typhus fever of Mexico (Wolbach and Todd: *Jour. Inf. Dis.*, July, 1915, p. 1). The organism has been seen in 13 instances in skin excised from patients during life and in 22 instances in tissues obtained at autopsy. The most easily demonstrable form of the organism occurs in clumps; the individual organisms are pairs of slightly elongated bodies with tapering ends. They are surrounded by an unstained area. The length of a paired

organism is from 1 to 1.5 microns. Isolated pairs and groups of several pairs are found with considerable frequency in swollen endothelial cells both in relation to thrombi and remote from lesions; they are found both in tissues taken during life and in material obtained shortly after death. A second form of the organism, occurring much less frequently, is a minute paired granule which fills endothelial cells while they are still *in situ*. In skin excised during life and in tissues obtained at autopsy, peculiar swollen and vacuolated endothelial cells are seen; in the authors' experience, they occur only in typhus. In them are numerous granules, which often completely fill the cell. The granules are very small; they are at the limit of visibility. They are being studied as a possible third form of the parasite. All forms of the organism stain blue. The larger paired forms are deeply colored; the other forms retain the stain less densely. Typhus was transmitted to guinea-pigs by the inoculation of infected lice. The disease runs the recognized course in infected animals. Characteristic lesions occur in the brain. The testes and epididymis often show an occasional vessel with lesions of the intima, thrombi and perivascular reaction quite similar to those observed in patients. The larger forms of the organism as seen in man have already been found in the lesions of cerebral vessels in the guinea-pig. Great pains were first taken to be sure that the stock lice used in the experiments were uninfected. It was found that the organisms were acquired by these lice when fed upon cases of typhus fever during the first ten days of the disease. The organisms are consistent in their characteristics with those described by da Rocha Lima as Rickettsia prowazeki (Da Rocha Lima: *Deutsch. med. Wchnschr*, July 3, 1919, p. 732). They are exceedingly pleomorphic. They vary in form from a minute, paired body to a bacilliform organism measuring several microns in length; both the minute and the bacillary forms occur in chains; the chains of bacilliform organisms often measure more than 15 microns in length. The organisms may be present in infected lice in extraordinary numbers. Every epithelial cell lining a louse's gut may be enormously distended by myriads of organisms, and through the bursting of the cells many organisms may be set free into the lumen of the gut. The distended cells of a heavily infected louse can be easily seen with a low magnification (objective 16 mm.) or even unstained with a dissecting microscope. All forms of the organism may be present in the distended cells of a heavily infected midgut; but the small forms occur most frequently and, as a rule, occur in cells that are most distended. The authors have formed the impression that the bacillary phase occurs early in the infection of a cell and that the minute form of the organism is characteristic of an advanced cell infection. As a rule, all organisms, whether intracellular or free in the lumen of the alimentary tract, stain blue; occasionally, organisms free in the gut are colored red, possibly because of variations in technic. The authors state in conclusion that in lice fed upon typhus patients under conditions determined to be favorable a peculiar, pleomorphic microörganism is constantly present. This microorganism is that named by da Rocha Lima Rickettsia prowazeki. In the vascular lesions of man and experimental animals infected with typhus a minute microörganism has been demonstrated. In morphology and staining reactions it is consistent with Rickettsia prowazeki in at least two of the forms in which it is seen constantly in lice.

Influence of Smallpox and Vaccination on Pulmonary Tuberculosis.—Howk and Lawson (*Am. Rev. Tuberc.*, September, 1920, No. 7, iv, 490) record an epidemic of smallpox occurring in the Metropolitan Life Insurance Company Sanatorium in the autumn of 1914. Time was purposely allowed to intervene between the epidemic and the writing of a formal record of it in order that the observations might show, not alone the immediate effects, but some of the remote influences of smallpox on pulmonary tuberculosis as well. There have been few similar experiences reported, nor is more than brief mention made in any of the writings on exanthematous diseases of the possible or probable effect that smallpox may have on clinical tuberculosis, although the literature is quite replete with reports of certain other concurrent complications of pulmonary tuberculosis. There were 7 cases of pulmonary tuberculosis which contracted smallpox, all of which recovered. In 1 case there was a moderately severe bronchitis following the onset of smallpox. There was no development of pneumonia in any case. The smallpox was of a mild form in 6 cases, severe in one, and its course was apparently unaffected by the presence of tuberculosis. The one outstanding feature of the tuberculosis following smallpox was the marked diminution of expectoration in two advanced, active cases. The effect was more striking than anything witnessed in tuberculosis, except the reduction following artificial pneumothorax. In 1 case there has never been any return of sputum or bacilli, although the patient had extensive basal lesions. In the other the sputum and bacilli were absent for four months. The authors conclude that smallpox, occurring in patients with pulmonary tuberculosis, runs a course not noticeably different from that encountered in well people. The symptomatology, appearances of exanthem, and duration of the smallpox are not influenced by the presence of tuberculosis. In early, inactive cases of tuberculosis with favorable prognosis there is no apparent interruption of recovery when complicated by smallpox. In 1 active advanced case there was a disappearance of sputum and bacilli after smallpox, lasting for four months. In one very very active and advanced case there was a permanent disappearance of sputum and bacilli immediately after the smallpox. The disease was progressive up to the time of smallpox and retrogressive thereafter. The 7 recovered from smallpox and 6 are alive and well at present. The presence of tuberculosis does not affect the normal course of vaccinia. Tuberculosis in any stage or any degree of activity was not affected by vaccination, either favorably or unfavorably.

Notice to Contributors.—All communications intended for insertion in the Original Department of this Journal are received only *with the distinct understanding that they are contributed exclusively to this* Journal

Contributions from abroad written in a foreign language, if on examination they are found desirable for this Journal, will be translated at its expense.

A limited number of reprints in pamphlet form, if desired, will be furnished to authors, *providing the request for them be written on the manuscript.*

All communications should be addressed to—

Dr. George Morris Piersol, 1913 Spruce St., Philadelphia, Pa., U. S. A.

"Just What a Ligature Should Be"

Armour's Surgical Catgut Ligatures, plain and chromic, Emergency (20 in.), Regular (60 in.) lengths.

Sizes ooo to Number 4 inclusive.

Smooth, strong and sterile.

Iodized **Catgut Ligatures.**

Smooth, strong, sterile and very pliable, 60 inch lengths only.

Sized oo to Number 4 inclusive.

Made from stock selected in the abattoirs especially for surgical purposes.

Pituitary Liquid (Armour) ½ c. c. (obstetrical), 1 c. c. (surgical), oxytocic and stimulant. Free from preservatives.

Endocrine Gland and Organotherapeutic Products.

Literature to pharmacists, physicians and hospitals on request.

ARMOUR AND COMPANY
CHICAGO

We are producing an
Arsphenamine *and a* Neoarsphenamine
than which no better products are made anywhere in the world

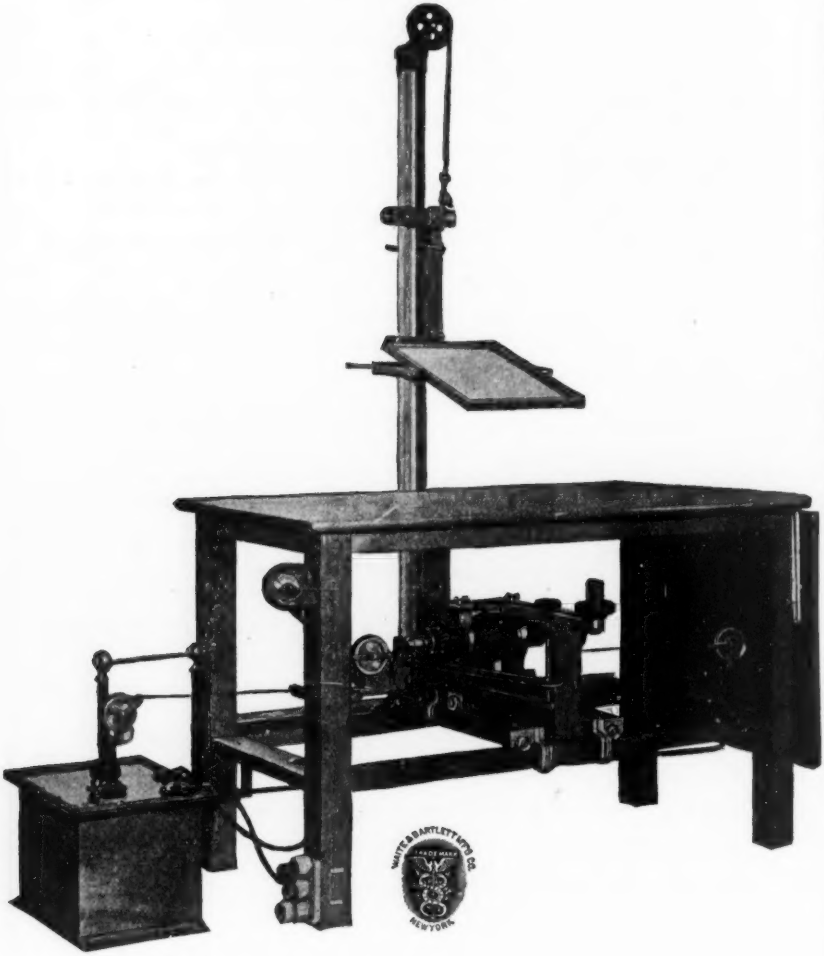
Recent studies carried on in the U.S.P.H.S. Laboratories at Washington comparing the toxicity of the American and Foreign Arsphenamines and Neoarsphenamines demonstrate that the American products exhibit a lower toxicity.

Analogous studies made in our own laboratories give similar results.

Our Neoarsphenamine is rapidly soluble and may be administered in 5 c.c. of water. It is splendidly tolerated and produces admirable clinical and serological results.

DERMATOLOGICAL RESEARCH LABORATORIES
1720-22 Lombard Street and 1713-15-17-19-21-23 Naudain Street
PHILADELPHIA

HORIZONTAL TABLE AND THE U. S. ARMY BEDSIDE TRANSFORMER



WAITE & BARTLETT MFG. CO.

53 JACKSON AVENUE, LONG ISLAND CITY, N. Y.

Showroom: 103 PARK AVENUE, NEW YORK CITY

California Agents: Gagan-Richardson Co., 127 E. 6th St., Los Angeles, California

(See opposite page)

FLUOROSCOPY is acknowledged by all recent writers to be the most important single diagnostic aid in chest and gastric intestinal examinations. However, until this simple unit (using the wonderful United States Army Bedside Transformer, which has revolutionized *X*-ray Work) was put on the market, the apparatus was expensive, bulky, required special electric service, and in addition required considerable technical skill to operate it. This new unit, however, does away with all of these objections. No electrical or mechanical training is required. Floor space 24 inches wide, 20 inches deep, any lamp socket will supply the current. There is now no reason why every Internist cannot do his own Fluoroscopy in his Office.

OURSELVES AND OTHERS

We have been established since 1879, and are now, as then, among the leaders in bringing out the best and most up-to-date apparatus. We have always striven to eliminate *unnecessary* size, cost and complexity in our apparatus. Soon all the cumbrous tables and vertical fluoroscopes will be a drug on the market, and compact, convenient installations will be the order of the day as in the case of our U. S. Army Bedside Unit and our Radiographic Dental Unit.

Some dealers do not push our goods because we do not allow so large a discount as other manufacturers. When the name of Waite & Bartlett is mentioned they begin to talk about *service*, that being the easiest way to counteract the good points of the Waite & Bartlett apparatus.

Our apparatus is in use all over the world, a fact which justifies our claim that our apparatus does *not require* the attention of a *service* man every little while.

WAITE & BARTLETT MFG. CO.

53 JACKSON AVENUE, LONG ISLAND CITY, N. Y.

Showroom: 103 PARK AVENUE, NEW YORK

California Agents: Gagan-Richardson Co., 127 E. 6th St., Los Angeles, California

AN IDEAL ARSENICAL

SODIUM DIARSENOL

SODIUM ARSPHENAMINE

SODIUM DIARSENOL marks a distinct advance in syphilology. It dissolves very quickly in water, giving a solution ready for immediate injection. No addition of sodium hydroxide is necessary. It has the therapeutic advantage of arsphenamine with the solubility and convenience of neoarsphenamine, and gives clinical results equal to or better than either of the two latter compounds. Neutralization with alkali being obviated, there is no undue handling and consequent decomposition of the highly reactive solution.

SODIUM DIARSENOL has been accepted by the council on Pharmacy and Chemistry of the American Medical Association for inclusion in "New and Nonofficial Remedies."

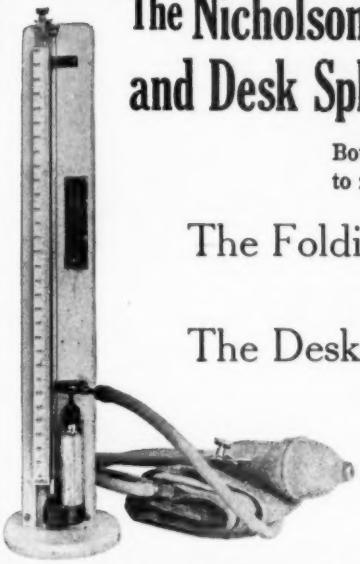
Manufactured by Diarsenol Laboratories, Inc., Buffalo, N. Y., under license from The Chemical Foundation, Inc., under patents 1059983 and 1078135.

Samples and literature on request

DIARSENOL COMPANY

INCORPORATED

BUFFALO BOSTON ATLANTA



The Nicholson Princo Mercurial Folding and Desk Sphygmomanometers

Both graduated to 300 mm., and easily adjusted to zero reading

The Folding Instrument $30.00
Type "B"

The Desk Instrument $25.00
In White Enamel

Our booklet entitled "Blood Pressure" and a pamphlet on "The Clinical Significance of Diastolic and Pulse Pressure" by Percival Nicholson, M.D., will be cheerfully mailed upon request

PRECISION THERMOMETER & INSTRUMENT CO. 1434 Brandywine St. Philadelphia, Pa.

Radium

SALTS (Purity as specified).

NEEDLES—Invaluable in certain malignant conditions).

UNIVERSAL APPLICATORS (Gold, silver, etc. Shape tubular).

FLAT APPLICATORS (Size and Radium content as desired).

EMANATION APPARATUS INSTALLATIONS.

COMPLETE clinical data in respect to dosage, technic, etc. Immediate deliveries to U.S. Bureau of Standards for measurement. Full particulars on request.

The W. L. Cummings Chemical Co.

WORKS AND LABORATORIES

LANSDOWNE PHILADELPHIA

RADIUM

TUBULAR APPLICATORS—NEEDLE APPLICATORS—FLAT APPLICATORS
and APPLICATORS *of* SPECIAL DESIGN

COMPLETE INSTALLATIONS *of* EMANATION APPARATUS

Sold on Basis of U. S. Bureau of Standards Certificate

Correspondence invited by our Physical, Chemical and Medical Departments

THE RADIUM COMPANY OF COLORADO, INC.
Main Office and Reduction Works—DENVER, COLORADO, U. S. A.

BRANCH OFFICES
108 N. State Street, Chicago
50 Union Square, New York
LONDON
PARIS

THE GLEN SPRINGS

On Seneca Lake
OPEN ALL YEAR

WATKINS, N. Y.

WM. E. LEFFINGWELL
President

A MINERAL SPRINGS HEALTH RESORT AND HOTEL

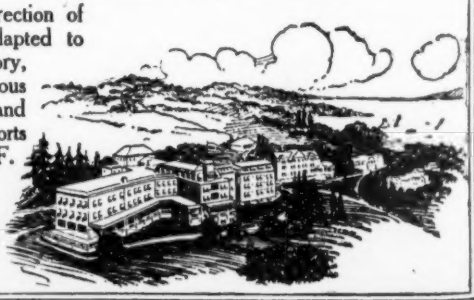
IN THE HEART OF THE FINGER LAKES REGION

The Pioneer American "Cure" for Heart Disorders

The only place in this country where the Nauheim Baths for Heart and Circulatory Disorders are given with a Natural Calcium Chloride Brine

Hydrotherapy, Electrotherapy, Massage

The treatments under the direction of physicians are particularly adapted to HEART DISEASE, Circulatory, Kidney, Nutritional and Nervous Disorders, Rheumatism, Gout and Obesity. Splendid facilities for sports and recreations. FINE GOLF.



Physicians are requested to send for literature detailing treatments, Mineral Springs analyses and other particulars.

A study of yeast dosage

THE question of yeast dosage is naturally of immediate interest to those physicians who have followed the results of the investigations of the therapeutic value of yeast by Dr. Philip B. Hawk and his collaborators, as reported in the Journal of the American Medical Association for Oct. 13, 1917.

In the tests made at Jefferson Medical College and in the cases treated at the Philadelphia General Hospital and the Roosevelt Hospital in New York, the usual dosage in treatment of furunculosis, the acnes, and constipation, was one cake of yeast administered t. i. d., in suspension in water, fruit-juices or milk.

The menstruum, however, is not important. Yeast may be dissolved in any liquid according to the preference of the patient; it may also be eaten plain in the cake or may be spread on cracker or bread, buttered or unbuttered.

In a very few cases the usual dosage of one cake three times daily was reduced to half a cake three times daily. The laxative tendency of the yeast is more pronounced in some cases than in others and the physician will, of course, regulate the dosage from a maximum of three cakes daily in accordance with the laxative effect produced.

The comparative effects of doses of "living" and "dead" yeast were closely studied. The yeast was "killed" by dissolving it with boiling water for a few minutes. The tests showed that killed yeast has the same therapeutic action as living yeast. If the patient is troubled with gas formation, it is preferable to use killed yeast, or to administer living yeast between meals.

The remarkable curative properties of yeast have long been recognized by physicians, but yeast as formerly used was hard to get, variable in quality, and uncertain in action.

The objectionable features of yeast in earlier and other forms are obviated by the scientificially perfect compressed yeast prepared by the Fleischmann Company.

This yeast is of the species Saccharomyces Cerevisiae, scientifically cultured, and kept free from contamination by wild yeast or other impurity.

Never touched by hands in the making, it goes through apparatus continually submitted to live steam for sterilization. The final wrapping—and even the cutting of the wrapper—is performed by scrupulously clean machinery.

Fleischmann's Yeast may be secured fresh, daily, from grocers. If the physician prefers, he may write to the Fleischmann Company in the nearest large city and it will be mailed direct on the days wanted.

THE FLEISCHMANN COMPANY

701 Washington St., New York, N. Y.
941-945 Mission St., San Francisco, Cal.
327 S. La Salle St., Chicago, Ill.
508 Green Building, Seattle, Wash.
208 Simcoe St., Toronto, Canada.

Adrenalin in Medicine

5—In Combination with Local Anesthetics

THE importance of Adrenalin in the induction of local anesthesia can be estimated by a realization of the fact that one of the major prerequisites of an efficient local anesthetic is that it be compatible with Adrenalin.

In the rôle of synergist to the anesthetic Adrenalin serves a threefold purpose; it blanches the tissues, giving the surgeon a clear field of operation; it confines the anesthetic to the area into which it is infiltrated, preventing absorption and possible toxic manifestations; it intensifies and prolongs the anesthesia by diminishing the circulation, thus obviating the dilution, oxidation and rapid destruction of the anesthetic in the tissues.

The question of the quantity of Adrenalin to be injected with the local anesthetic solution deserves special consideration on the part of the surgeon. It should be remembered that after the effects of the injection of a *large* dose of Adrenalin have been dissipated, after the local ischemia has subsided, the patient is liable to have a secondary hemorrhage, owing to a reaction in the walls of the vessels which manifests itself in obstinate dilatation. Many instances of sloughing are attributable to the strangulation ensuing upon the injection of too much Adrenalin. It is incumbent upon the surgeon, therefore, to regulate carefully the Adrenalin content of the anesthetic solutions he employs.

In laparotomies and other major operations in which an ounce or more of anesthetic solution is required the proportion of Adrenalin need not exceed 1 in 100,000. This concentration can be approximated by adding five drops of the 1:1000 Adrenalin to the ounce of anesthetic solution. When smaller quantities are to be injected it is permissible to increase the Adrenalin proportion to 1:50,000 or 1:40,000.

The most satisfactory results are obtained by first sterilizing (boiling) the anesthetic solution and then, after it has partly cooled, to add the requisite number of drops of Adrenalin 1:1000. This permits of gratifying flexibility; the surgeon is enabled to vary the proportion of Adrenalin in the anesthetic fluid at will and with a minimum of inconvenience.

PARKE, DAVIS & COMPANY

Arsphenamine Products Should Be:

Readily Soluble
Practically Free From Toxicity
Easy of Administration

NEOSALVARSAN

(NEOARSPHENAMINE–METZ)

Possesses all of these qualities

Order by either name and if your local dealer cannot supply you order direct from

H. A. METZ LABORATORIES, INC.
122 Hudson Street
New York

WINTHROP SYNTHETICS

CONFORM TO ORIGINAL HIGH STANDARDS

Veronal
Adalin
Luminal } Hypnotics and Sedatives

Novaspirin
Salophen
Mesotan } Antirheumatics and Analgesics

Sajodin Palatable Organic Iodine
Elarson Agreeable Organic Arsenic
Protargol Antigonorrheic
Helmitol Urinary Antiseptic

Also: **Coryfin, Tannigen, Duotal, Creosotal, Heroin, Aristol, Phenacetin, Sulfonal, Trional, Cymarin, Hydrastinin**

Literature on Request

WINTHROP CHEMICAL COMPANY, Inc.
189-191 Franklin Street, New York, N. Y.

BENZYL ALCOHOL—IPCO

This product complies with the N. N. R. standards

It is a VEN sterile solution, 4 per cent. in 2 c.c. of physiologic sodium chlorid solution, and is ready for immediate use

Of 250 VEN Products in IPCO Ampoules, the popular ones are

VEN—Sodium Iodide No. 41, 15 gr.—No. 42, 30 gr.
VEN—Hexamethylenamine No. 23[A], 31 gr.
VEN—Quinine, 7.5 gr.
VEN—Caffeine No. 51[B], 3.75 gr.—No. 51[C], 7.5 gr.
Camphor in Oil or Ether, all doses
Strophanthin, all doses

Intra Products Company

Denver, Colorado

Palatable

Benzyl Benzoate 20%

AROMATIZED SUSPENSION

(Made from VAN DYK & CO. brand)

Jour. Am. Med. As., Oct. 16, 1920, Page 1069

Antispasmodic in ASTHMA and DYSMENORRHEA

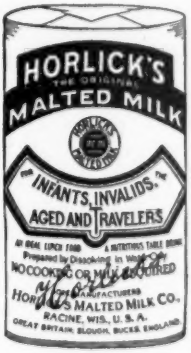
OUR SUSPENSION IS PREFERABLE
because it is:

NON-ALCOHOLIC
READILY MISCIBLE with WATER
RARELY REGURGITATES
PLEASANT to the EYE

Write for Clinical Data

United Synthetic Chemical Corporation
4 Platt Street **New York, N. Y.**

AVOID IMITATIONS



PRESCRIBE THE ORIGINAL PRODUCT OF RELIABLE QUALITY

100 Million Explosions

In a Grain of Wheat

Puffed Wheat is whole wheat steam exploded. The grains are sealed in guns. After an hour of fearful heat the guns are shot. And over 100 million steam explosions are caused in every kernel.

The process was invented by Prof. A. P. Anderson, to make whole grains wholly digestible, and easy to digest.

Puffed Rice is whole rice puffed in like way. Corn Puffs are corn hearts puffed.

These bubble grains, flimsy and nut-like, form most delicious foods. And they are the best-cooked cereals in existence.

Puffed Wheat
Puffed Rice
Corn Puffs

Volume I Now Ready. Volume II, Shortly

Surgical Diagnosis and Treatment

BY EMINENT SURGICAL AUTHORITIES

EDITED BY

ALBERT J. OCHSNER, M.D., F.A.C.S.

Professor of Surgery in the University of Illinois; Surgeon-in-Chief to the Augustana and St. Mary's Hospitals, Chicago, Ill.

Four octavo volumes of about 850 pages each, with over 2000 illustrations, many in colors. Cloth, per set, $40.00, net; in Canada, $45.00, net

"THE GREATEST SURGERY OF ALL TIME"

is what we believe you will call this work, for seventy-six of America's greatest surgeons have written it.

It in every sense *reflects the current practice and thought of the most intensely active surgeons of this continent.* Its chapters tell the *why* and *how* in the solution of each surgical problem, *what to do and what to avoid.* It brings you in touch with the *actual experience, reasoning and practical methods* of men eminent in all parts of the country. Each one describes intimately his methods of diagnosis, his plans for treatment before and after operation and gives his judgment regarding them. This monumental work gives you the opinions *not of one man,* but the *combined experience, skill and advice of seventy-six of our foremost surgeons.*

Each man writes on the field in which he has achieved greatest success and fame

You will find nothing here that smacks of what is copied from text-books; but only fresh material that represents the living work of today done by those who are the outstanding surgical authorities of the country. The illustrations are almost, if not quite, as important as the text, so illuminating are they. Time and time again you will find *whole series devoted to the detailed disclosure of each step of a particular operation.* The technique of difficult procedures is made wonderfully clear and easily grasped through these admirable illustrations. Thoroughness is the keynote of the entire work. No expense or pains have been spared in its preparation. Proofs have been revised and again revised to insure smoothness of diction and the inclusion of all up-to-date material up to the very minute of going to press. Destined to be the Standard American Authority on Surgery, this work should find a place in the library of every Practitioner, Specialist and Surgeon for its value in daily use and as *THE* authoritative reference.

(See Opposite Page)

706-8-10 Sansom St. PHILADELPHIA

LEA & FEBIGER

PUBLISHERS

2 W. 45th Street NEW YORK

THE EMINENT CONTRIBUTORS

(*See Opposite Page*)

ABBE, ROBERT, M.D.
ALBEE, FRED H., M.D., F.A.C.S.
ANDREWS, E. WYLLYS, A.M., M.D.
ARCHIBALD, ALEXANDER, M.D., CH.B. (EDIN.).
ARMSTRONG, GEORGE E., M.D., F.A.C.S.
ASHHURST, ASTLEY P. C., M.D., F.A.C.S.

BECK, CARL, M.D., F.A.C.S.
BECK, EMIL G., M.D., F.A.C.S.
BECK, JOSEPH C., M.D., F.A.C.S.
BINNIE, JOHN FAIRBAIRN, F.A.C.S.
BOTTOMLEY, JOHN TAYLOR, M.D., LL.D.
BRADFORD, E. H., M.D., F.A.C.S.
BRAASCH, W. F., B.S., M.D.
BREWER, GEORGE EMERSON, M.D., LL.D.
BROWN, GEORGE VAN INGEN, M.D., F.A.C.S.
BRUCE, HERBERT A., M.D., F.R.C.S., ENG.
BUERGER, LEO, M.D., M.A., F.A.C.S.

CLARK, JOHN G., M.D.
CRILE, DENNIS W., B.S., M.D.
CRILE, GEORGE W., M.D., F.A.C.S.
CUNNINGHAM, JOHN H., M.D.
CUSHING, HARVEY, M.D., SCD., F.R.C.S.

DA COSTA, JOHN CHALMERS, M.D., LL.D.
DAVIS, CARL B., M.D.
DEAVER, JOHN B., M.D.

ESTES, WILLIAM L., M.A., M.D.
ESTES, WILLIAM L., JR., B.A., M.D.

FAY, OLIVER J., S.B., M.D., F.A.C.S.
FINNEY, J. M. T., M.D.
FREEMAN, LEONARD, M.D.

GIBBON, JOHN H., M.D.
GREENOUGH, ROBERT B., M.D.

HAGGARD, WILLIAM D., M.D., F.A.C.S.

JACKSON, CHEVALIER, M.D.
JONAS, A. F., M.D.

KAHLKE, CHARLES EDWIN, M.D., F.A.C.S.
KANAVEL, ALLEN B., M.D.

LEWIS, DEAN, M.D.
LILIENTHAL, HOWARD, M.D., F.A.C.S.

McKECHNIE, ROBERT E., M.D., F.A.C.S.
McLEAN, ANGUS, M.D., F.A.C.S.
McWILLIAMS, CLARENCE A., M.D., F.A.C.S.
MacCARTY, WILLIAM CARPENTER, M.D.
MACKENZIE, KENNETH A. J., M.D., F.A.C.S.
MacLAREN, ARCHIBALD, M.D., F.A.C.S.

MARTIN, FRANKLIN H., M.D., F.A.C.S.
MATAS, RUDOLPH, M.D., F.A.C.S.
MAYO, WILLIAM J., M.D., F.A.C.S.
MEYER, WILLY, M.D.
MURPHY, FRED T., M.D.

NADEAU, OSCAR E., B.S., M.D.
NUZUM, JOHN W., S.B., M.D.

OCHSNER, ALBERT J., M.D., F.A.C.S.

PERCY, NELSON MORTIMER, M.D., F.A.C.S.
PFEIFFER, DAMON B., M.D.
PILCHER, JAMES TAFT, M.D.
PILCHER, LEWIS STEPHEN, M.D., LL.D.
POLLOCK, LEWIS J., M.D.
POWERS, CHARLES A., A.M., M.D.
PUSEY, WILLIAM ALLEN, M.D.

RANSOHOFF, J. LOUIS, M.D., F.A.C.S.
RANSOHOFF, JOSEPH, M.D., F.A.C.S.
RISLEY, EDWARD HAMMOND, M.D., F.A.C.S.
RITCHIE, HARRY P., M.D., F.A.C.S.
RODMAN, J. STEWART, M.D.
RODMAN, WILLIAM L., M.D.

SCHIFFBAUER, H., M.D. F.A.C.S.
SCHMIDT, ERWIN R., B.A., M.D.
SCHMITZ, HENRY, M.D., F.A.C.S.
SHAMBAUGH, GEORGE E., M.D.
SHERMAN, HARRY M., M.D.
SMITHIES, FRANK, M.D., F.A.C.P.
SOUTTER, ROBERT, A.B., M.D.
STANTON, E. MacD., M.D., F.A.C.S.
STURM, MEYER J., B.S.

TINKER, MARTIN B., M.D.

WEISENBURG, THEODORE H., M.D.

PUBLIC HEALTH AND HYGIENE

By Eminent Authorities

Edited by WILLIAM HALLOCK PARK, M.D.

Professor of Bacteriology and Hygiene, University and Bellevue Hospital Medical College; Director of the Bureau of Laboratories, Department of Health, New York City

Octavo, 884 pages with 123 illustrations. Cloth, $10.00, net

THE growing opinion that **public health is to a large extent purchasable** has stimulated health authorities to develop their opportunities and to assume greater responsibilities. The best medical colleges no longer confine their teaching to the diagnosis and treatment of disease, but give thorough courses in hygiene, and its practical application in preventive medicine. The technological schools are providing similar courses.

The great advances in hygiene and the increasing scope of public health work have led to the creation of many subdivisions and the problems and practices connected with these have become so highly technical as to require public health workers to restrict their activities to special lines. The medical officer for some time has appreciated this. Wherever the community is large enough to afford it, he has obtained **the service of specialists.** The department of health of any progressive State or large city has under the administrative head a number of bureaus, each of these under some specialist who has demonstrated his fitness.

The time has passed when any one person can possess the technical knowledge and personal experience required properly to direct and develop all or even several of these different branches of public health work. There was need **of a volume in which the most important phases of hygiene in relation to public health would be presented in a practical way by specialists actually devoting themselves to the subjects treated by them.** This book is intended for public health officials, physicians and medical students, and each contributor has therefore made his section as practical as possible and utilized to the full his own personal experience.

CONTENTS

Relation of Microörganisms to Disease, Wm. H. Park, M.D.

Antimicrobal or Antiprotein Substances Individually Considered, Wm. H. Park, M.D., and Charles Krumwiede, M.D., Assistant Director of the Bureau of Laboratories, New York City.

Prevention of Individual Infectious Diseases, Wm. H. Park, M.D.

Practical Use of Disinfectants, Wm. H. Park, M.D.

Epidemiology, Geo. A. Soper, Ph.D., Major, Sanitary Corps, U. S. A.

Sanitary Surveys, W. L. Dodd, Assistant Director, Department of Sanitation of the Pease Laboratories, N. Y.

Air and Health—Ventilation, C. E. A. Winslow, Dr. P. H., Professor of Public Health, Yale School of Medicine.

Housing, Lawrence Veiller, Secretary of the National Housing Association, N. Y.

Food, Edward K. Dunham, M.D., Lt.-Col., Medical Corps, U. S. A.

Vitamines, Alfred F. Hess, M.D., Clinical Professor of Pediatrics, New York University and Bellevue Hospital Medical College.

The Preservation and Adulteration of Food, J. P. Atkinson, M.S., Chief Chemist, Department of Health, N. Y.

Bacterial and Other Contaminations of Milk, Their Relation to Public Health, Wm. H. Park, M.D.

Bacterial Infections and Parasitic Diseases from Milk, Meat and Other Foods, Wm. H. Park, M.D.

The Soil, Arthur R. Guerard, M.D., Lecturer on Social Hygiene, New York State Department of Health.

Water Supplies and Their Purification. James T-B. Bowles, B.S., Lecturer in Water Supply and Sewage Disposal, New York University, Department of Hygiene, Bellevue Hospital Medical College; formerly in charge of Water Supplies and Purification Plants, Canal Zone, Panama.

Sewage and Waste Disposal, James T-B. Bowles, B.S.

Housing and Plumbing, Arthur R. Guerard, M.D.

The Sanitation of Swimming Pools. Wallace A. Manheimer, Ph.D., Vice-President of the International Congress on Public Baths, Belgium, 1920.

Personal Hygiene, Eugene Lyman Fisk, M.D., Medical Director of the Life Extension Institute, New York.

Additional Practical Points in Personal Hygiene, Arthur R. Guerard, M.D.

Military Hygiene, C. W. Berry, M.D., Lecturer on Military Hygiene, New York University and Bellevue Medical College, Brigadier-General, N. Y. National Guard.

Rural Public Health Work, Frank Overton, M.D., P.H., Sc.C., Sanitary Supervisor, N. Y. State Dept. of Health.

Tropical Hygiene, M. F. Connor, M.D., Health Officer, Panama Canal, 1904–1914; Senior State Director, International Health Board.

Industrial Hygiene, Louis I. Harris, M.D., Director of Bureau of Preventable Diseases, N. Y. City; Medical Advisor to the Labor Sanitation Conference, Greater New York.

Child Hygiene, S. Josephine Baker, M.D., D.P.H., Director of Bureau of Child Hygiene, Department of Health, New York; Consultant in Child Hygiene, U. S. Public Health Service.

Sociologic and Economic Aspects of Disease, Charles F. Bolduan, M.D., Chief of the Section of Public Health Education, U. S. Public Health Service.

Public Health Education, Charles F. Bolduan, M.D.

Mental Hygiene, August Hoch, M.D., late Director, Psychiatric Institute, Manhattan State Hospital for the Insane, New York.

Mental Defectives, Preventing and Controlling Measures, Henry H. Goddard, Ph.D., Director of Bureau of Juvenile Research, Columbia, O.

Maritime Quarantine, Leland E. Cofer, M.D., Health Officer of the Port of New York.

Vital Statistics, William H. Guilfoy, M.D., Registrar of Records, Department of Health, New York and Shirley W. Wynne, M.D., Chief of Division of Statistical Research, Department of Health, New York.

706-8-10 Sansom St. PHILADELPHIA

LEA & FEBIGER

PUBLISHERS

2 W. 45th Street NEW YORK

THE BATTLE CREEK SANITARIUM AND HOSPITAL

Established 1866

MEDICAL OBSTETRICAL ORTHOPEDIC
NEUROLOGICAL SURGICAL RECONSTRUCTIVE

EDUCATIONAL DEPARTMENTS

Training School for Nurses Normal School of Physical Education
School of Home Economics and Dietetics

Students received on favorable terms. Registered trained nurses, dietitians and physical directors supplied.

DESCRIPTIVE LITERATURE MAILED FREE UPON REQUEST

THE BATTLE CREEK SANITARIUM
BATTLE CREEK Box 247 MICHIGAN

To stabilize the alkaline reserve

in the acute infections (including influenza and pneumonia) large quantities of alkali are needed.

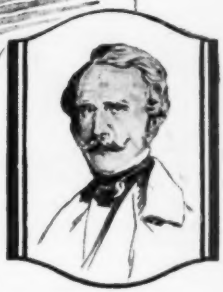
If their administration offers difficulty

PRESCRIBE KALAK WATER

Each bottle carries in sparkling form several grammes of the bicarbonates of sodium, potassium, calcium and magnesium.

Kalak Water Company of N.Y.
23 City Hall Place New York City

Dr. William T. G. Morton Elected to Hall of Fame



THE Nujol Laboratories of the Standard Oil Co. (New Jersey) recently conducted a referendum vote among all physicians and surgeons in the United States, a list of some 140,000, sending to each a booklet entitled "Medical Nominations for the Hall of Fame 1920" containing a biographical sketch of each of the twelve medical men whose names had been nominated for election to the Hall of Fame.

The returns when received were tabulated and communicated to the authorities in charge of the election to the Hall of Fame.

The entire medical profession will be gratified that the memory of Dr. Morton has been honored by his election to a place among this group of distinguished Americans comprising the Hall of Fame.

We believe that the widespread interest shown by the medical profession in our ballot and in the general election contributed to no small extent in securing long deferred recognition of the achievements of medical science in the United States.

Nujol

REG. U.S. PAT. OFF.

VOL. CI

1820

AN
TH

ACUTE
DAV
WHOOP
TW
EXPERI
FU
OF
RETENT
SU
THE B
BA
LEUKE
GE
THE C
CLASS
WE
MULTI
PE
NEPH
INFEC
M
URINA
R
THE P
T
AMNE
INTER
INDEX

Phil

COPYRIGHT